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=> d que stat l26
L20           1 SEA FILE=REGISTRY ABB=ON  Δ8-TETRAHYDROCANNABINOL/CN
L21           2 SEA FILE=REGISTRY ABB=ON  (CANNABINOL OR CANNABIDIOL)/CN
L22           3 SEA FILE=REGISTRY ABB=ON  L20 OR L21
L23        5906 SEA FILE=HCAPLUS ABB=ON  L22 OR (Δ8-TETRAHYDROCANNABINOL?
                 OR ?CANNABINOL? OR ?CANNABIDIOL?)
L24          68 SEA FILE=HCAPLUS ABB=ON  L23 AND (?BLASTOMA? OR ?EPITHELOMA?
                 OR ?GERMINOMA? OR ?CARCINOMA? OR ?ASTROCYTOMA? OR ?EPENDYMOMA?
                 OR ?OLIGODENROGLIOMA? OR ?OLIGODENDROGLIOMA? OR ?NEUROEPITHELOM
                 A? OR ?NEUROECTODERM?(W)(?TUMOR? OR ?TUMOUR?) OR ?MENINGIOMA?
                 OR ?SARCOMA? OR ?MELANOMA? OR ?SCHWANOMA?)
L25          29 SEA FILE=HCAPLUS ABB=ON  L24 AND (?THERAP? OR ?TREAT? OR
                 ?CURE? OR ?IMPROV?)
L26          26 SEA FILE=HCAPLUS ABB=ON  L25 AND (PRD<20030825 OR PD<20030825)

=> d ibib abs l26 1-26

L26  ANSWER 1 OF 26  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:60544  HCAPLUS
DOCUMENT NUMBER:          140:144682
TITLE:                    Molecular antigen arrays comprising AP205 virus-like
                          particle and antigen for prevention and
                          treatment of cancer, drug addiction,
                          poisoning, infection, and allergy
INVENTOR(S):              Bachmann, Martin F.; Tissot, Alain; Pumpens, Paul;
                          Cielens, Indulis; Renhofa, Regina
PATENT ASSIGNEE(S):       Cytos Biotechnology AG, Switz.
SOURCE:                   PCT Int. Appl., 170 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004007538         A2    20040122    WO 2003-EP7572           20030714 <--
     WO 2004007538         A3    20040304
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2489410            AA    20040122    CA 2003-2489410          20030714 <--
     US 2004076611         A1    20040422    US 2003-617876           20030714 <--
     EP 1532167            A2    20050525    EP 2003-763829           20030714 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003012935         A     20050621    BR 2003-12935            20030714 <--
PRIORITY APPLN. INFO.:                       US 2002-396126P      P   20020717 <--
                                             WO 2003-EP7572       W   20030714 <--
AB   The present invention provides a composition comprising an AP205 virus like
     particle (VLP) and an antigen. The invention also provides a process for
     producing an antigen or antigenic determinant bound to AP205 VLP. AP205
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VLP bound to an antigen is useful in the production of compns. for inducing immune responses that are useful for the prevention or **treatment** of diseases, disorders or conditions including infectious diseases, allergies, cancer, drug addiction, poisoning and to efficiently induce self-specific immune responses, in particular antibody responses.

L26 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472379 HCAPLUS
DOCUMENT NUMBER: 139:30794
TITLE: Method for the **treatment** of neoplasia
INVENTOR(S): Nagarkatti, Mitzi; Nagarkatti, Prakash; McKallip, Robert; Lombard, Catherine; Ryu, Seongho
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003049727	A1	20030619	WO 2002-US39310		20021209 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2468794	AA	20030619	CA 2002-2468794		20021209 <--
EP 1461027	A1	20040929	EP 2002-804754		20021209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005516004	T2	20050602	JP 2003-550776		20021209 <--
US 2004259936	A1	20041223	US 2004-497911		20040813 <--
PRIORITY APPLN. INFO.:			US 2001-336732P	P	20011207 <--
			WO 2002-US39310	W	20021209 <--

AB Method is disclosed for the **treatment** of patients with abnormality in cells of the immune system comprising administration of a **therapeutically** ED of a compound having CB2 cannabinoid receptor activity. The abnormality is particularly a malignancy such as a leukemia or lymphoma.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242184 HCAPLUS
DOCUMENT NUMBER: 138:285995
TITLE: Packaging of immunostimulatory substances and antigens into virus-like particles for use as vaccines against cancer, autoimmune disease, allergy and viral infection
INVENTOR(S): Maurer, Patrick; Tissot, Alain; Schwarz, Katrin; Meijerink, Edwin; Lipowsky, Gerad; Pumpens, Paul; Cielens, Indulis; Renhofa, Regina; Bachmann, Martin

F.; Storni, Tazio
PATENT ASSIGNEE(S): Cytos Biotechnology A.-G., Switz.
SOURCE: PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003024481	A2	20030327	WO 2002-IB4132		20020916 <--
WO 2003024481	A3	20040603			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2492826	AA	20030327	CA 2002-2492826		20020916 <--
US 2003099668	A1	20030529	US 2002-244065		20020916 <--
EP 1450856	A2	20040901	EP 2002-777600		20020916 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005517632	T2	20050616	JP 2003-528575		20020916 <--
PRIORITY APPLN. INFO.:			US 2001-318994P	P	20010914 <--
			US 2002-374145P	P	20020422 <--
			WO 2002-IB4132	W	20020916 <--

AB The invention relates to the finding that virus-like particles (VLPs) can be loaded with immunostimulatory substances, in particular with DNA oligonucleotides containing non-methylated C and G (CpGs). Such CpG-VLPs are dramatically more immunogenic than their CpG-free counterparts and induce enhanced B and T cell responses. The immune response against antigens optionally coupled, fused or attached otherwise to the VLPs is similarly enhanced as the immune response against the VLP itself. In addition, the T cell responses against both the VLPs and antigens are especially directed to the Th1 type. Antigens attached to CpG-loaded VLPs may therefore be ideal vaccines for prophylactic or **therapeutic** vaccination against allergies, tumors and other self-mols. and chronic viral diseases.

L26 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242183 HCAPLUS
DOCUMENT NUMBER: 138:270293
TITLE: Vaccine compositions comprising anti-CD4 antibody or immunostimulatory nucleic acid and antigen-coupled virus-like particles for enhancement of immune responses
INVENTOR(S): Bachmann, Martin F.; Storni, Tazio; Lechner, Franziska
PATENT ASSIGNEE(S): Cytos Biotechnology A.-G., Switz.
SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024480	A2	20030327	WO 2002-IB4252	20020916 <--
WO 2003024480	A3	20031030		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2492823	AA	20030327	CA 2002-2492823	20020916 <--
US 2003091593	A1	20030515	US 2002-243739	20020916 <--
EP 1425040	A2	20040609	EP 2002-783338	20020916 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

JP 2005507388	T2	20050317	JP 2003-528574	20020916 <--
PRIORITY APPLN. INFO.:			US 2001-318967P	P 20010914 <--
			WO 2002-IB4252	W 20020916 <--

AB The invention relates to the finding that stimulation of antigen presenting cell (APC) activation using substances such as anti-CD40 antibodies or DNA oligomers rich in non-methylated C and G (CpGs) can dramatically enhance the specific T cell response obtained after vaccination with recombinant virus like particles (VLPs) coupled, fused or otherwise attached to antigens. While vaccination with recombinant VLPs fused to a cytotoxic T cell (CTL) epitope of lymphocytic choriomeningitis virus induced low levels cytolytic activity only and did not induce efficient anti-viral protection, VLPs injected together with anti-CD40 antibodies or CpGs induced strong CTL activity and full anti-viral protection for **treating** tumors and chronic viral diseases. Thus, stimulation of APC-activation through antigen presenting cell activators such as anti-CD40 antibodies or CpGs can exhibit a potent adjuvant effect for vaccination with VLPs coupled, fused or attached otherwise to antigens.

L26 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2001:322837 HCAPLUS
DOCUMENT NUMBER:	135:132395
TITLE:	Characterization of palmitoylethanolamide transport in mouse Neuro-2a **neuroblastoma** and rat RBL-2H3 basophilic leukaemia cells: comparison with anandamide
AUTHOR(S):	Jacobsson, Stig O. P.; Fowler, Christopher J.
CORPORATE SOURCE:	Department of Pharmacology and Clinical Neuroscience, Department of Odontology, Umea University, Umea, SE-901 87, Swed.
SOURCE:	British Journal of Pharmacology (**2001**), 132(8), 1743-1754 CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The endogenous cannabinoid receptor agonist anandamide (AEA) and the related compound palmitoylethanolamide (PEA) are inactivated by transport into cells followed by metabolism by fatty acid amide hydrolase (FAAH). The

cellular uptake of AEA has been characterized in detail, whereas less is known about the properties of the PEA uptake, in particular in neuronal cells. In the present study, the pharmacol. and functional properties of PEA and AEA uptake have been investigated in mouse Neuro-2a **neuroblastoma** and, for comparison, in rat RBL-2H3 basophilic leukemia cells. Saturable uptake of PEA and AEA into both cell lines were demonstrated with apparent KM values of 28 μM (PEA) and 10 μM (AEA) in Neuro-2a cells, and 30 μM (PEA) and 9.3 μM (AEA) in RBL-2H3 cells. Both PEA and AEA uptake showed temperature-dependence but only the AEA uptake was sensitive to **treatment** with Pronase and phenylmethylsulfonyl fluoride. The AEA uptake was inhibited by AM404, 2-arachidonoylglycerol (2-AG), R1- and S1-methanandamide, arachidonic acid and olvanil with similar potencies for the two cell types. PEA, up to a concentration of 100 μM, did not affect AEA uptake in either cell line. AEA, 2-AG, arachidonic acid, R1-methanandamide, Δ9-THC, and **cannabidiol** inhibited PEA transport in both cell lines. The non-steroidal anti-inflammatory drug indomethacin inhibited the AEA uptake but had very weak effects on the uptake of PEA. From these data, it can be concluded that PEA is transported in to cells both by passive diffusion and by a facilitated transport that is pharmacol. distinguishable from AEA uptake.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688060 HCAPLUS
DOCUMENT NUMBER: 133:247279
TITLE: Alkyl resorcinols, **cannabinols**, **cannabidiols**, and cannabigerols for **treatment** of diseases associated with immune dysfunction, viral infections, and neoplasms
INVENTOR(S): Travis, Craig R.
PATENT ASSIGNEE(S): Immugen Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056303	A2	20000928	WO 2000-US7629	20000322 <--
WO 2000056303	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2367262	AA	20000928	CA 2000-2367262	20000322 <--
AU 2000039107	A5	20001009	AU 2000-39107	20000322 <--
BR 2000009200	A	20011226	BR 2000-9200	20000322 <--
EP 1189603	A2	20020327	EP 2000-918266	20000322 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002539246	T2	20021119	JP 2000-606208		20000322 <--
ZA 2001007773	A	20030422	ZA 2001-7773		20010920 <--
PRIORITY APPLN. INFO.:			US 1999-125674P	P	19990322 <--
			US 1999-151595P	P	19990830 <--
			WO 2000-US7629	W	20000322 <--

AB The invention provides a method, compds., and compns. for **treating** a disease associated with immune dysfunction. A pharmacol.-acceptable composition including ≥1 compound selected from 5-alkyl-resorcinol derivs., **cannabinol** derivs., **cannabidiol** derivs., cannabigerol derivs., and combinations thereof, is administered to a patient under conditions sufficient to attenuate the dysfunction within the immune system. The invention also provides an antiviral **cannabinol** derivative that can be used in the method. The invention also provides an alkylated resorcinol derivative and a method of using the alkylated resorcinol derivative to attenuate the growth of a neoplasm. The method and compound are useful for **treating** diseases of the immune system, such as HIV disease and neoplastic disorders.

L26 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:493550 HCAPLUS
DOCUMENT NUMBER: 133:101736
TITLE: A reagent system and method for increasing the luminescence of lanthanide(iii) macrocyclic complexes
INVENTOR(S): Leif, Robert C.; Vallarino, Lidia
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042048	A1	20000720	WO 2000-US1211	20000118 <--
W: CA, CH, DE, FI, GB, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2360054	AA	20000720	CA 2000-2360054	20000118 <--
EP 1150985	A1	20011107	EP 2000-905653	20000118 <--
EP 1150985	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6340744	B1	20020122	US 2000-484670	20000118 <--
AT 270298	E	20040715	AT 2000-905653	20000118 <--
US 2002132992	A1	20020919	US 2001-10597	20011206 <--
US 6750005	B2	20040615		

PRIORITY APPLN. INFO.:		US 1999-116316P	P	19990119 <--
		US 2000-484670	A1	20000118 <--
		WO 2000-US1211	W	20000118 <--

OTHER SOURCE(S): MARPAT 133:101736
AB Disclosed are a spectrofluorimetrically detectable luminescent composition and processes for enhancing the luminescence of one or more lanthanide-containing macrocycles. The luminescent composition comprises a micelle-producing amount of at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compound having an emission spectrum peak in the range from 500 to 950 nm, and a luminescence-enhancing amount of at least one

energy transfer donor compound of yttrium or a 3-valent lanthanide element having atomic number 59-71, provided that the lanthanide element of said macrocycle compound and the lanthanide element of said energy transfer donor compound are not identical. The addition of gadolinium(III) in the presence of other solutes to both the prototype and the difunctionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patents #5,373,093 and #5,696,240, enhances their luminescence. Similar enhancements of luminescence also results for the mono-functionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patent #5,696,240. The enhanced luminescence afforded by the composition enables the detection and/or quantitation of many analytes in low concns. without the use of expensive, complicated time-gated detection systems.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:326272 HCAPLUS
DOCUMENT NUMBER: 133:100532
TITLE: Imprinting: perinatal exposures cause the development of diseases during the adult age
AUTHOR(S): Tchernitchin, A. N.; Tchernitchin, Nina N.; Mena, M. A.; Unda, Cristina; Soto, J.
CORPORATE SOURCE: Laboratory of Experimental Endocrinology and Environmental Pathology LEEPA, Institute of Biomedical Sciences ICBM and Environment and Biomedicine Research Center CIMAB, Medical School, University of Chile, Santiago, Chile
SOURCE: Acta Biologica Hungarica (**1999**), 50(4), 425-440
CODEN: ABHUE6; ISSN: 0236-5383
PUBLISHER: Akademiai Kiado
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with 121 refs. Since the early reports linking the development of clear cell cervicovaginal **adenocarcinoma** in young women with diethylstilbestrol **treatment** of their mothers during pregnancy, it became clear that perinatal exposure to several substances may induce irreversible alterations, that can be detected later in life. Current evidence suggests that these substances induce, by the mechanism of imprinting, alterations of the differentiation of several cell-types, resulting in the development of disease during the adult age. The most known delayed effects to prenatal exposure to agents displaying hormone action, pollutants, food additives and natural food components, substances of abuse and stress by the mechanism of imprinting are described. Among them, estrogens, androgens, progestins, lead, benzopyrenes, ozone, dioxins, DDT, DDE, methoxychlor, chlordecone, parathion, malathion, polychlorobiphenyls, pyrethroids, paraquat, food additives, normal food constituents, **tetrahydrocannabinol**, cocaine and opiates. It is concluded that perinatal exposure to several agents causes irreversible changes that determine health conditions during adulthood. Several diseases developing during adulthood probably were determined during early stages of life, under the effect of exposure or preferential mother's diet during pregnancy. Regulations to avoid these early exposures may contribute to an important **improvement** of health conditions of humankind.

REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:325337 HCAPLUS
DOCUMENT NUMBER: 133:38140
TITLE: The CB1 cannabinoid receptor is coupled to the activation of protein kinase B/Akt
AUTHOR(S): Del Pulgar, Teresa Gomez; Velasco, Guillermo; Guzman, Manuel
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: Biochemical Journal (**2000**), 347(2), 369-373
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cannabinoids exert most of their effects in the central nervous system through the CB1 cannabinoid receptor. This G-protein-coupled receptor has been shown to be functionally coupled to inhibition of adenylate cyclase, modulation of ion channels and activation of extracellular-signal-regulated kinase. Using Chinese hamster ovary cells stably transfected with the CB1 receptor cDNA we show here that Δ9-**tetrahydrocannabinol** (THC), the major active component of marijuana, induces the activation of protein kinase B/Akt (PKB). This effect of THC was also exerted by the endogenous cannabinoid anandamide and the synthetic cannabinoids CP-55940 and HU-210, and was prevented by the selective CB1 antagonist SR 141716. Pertussis toxin and wortmannin blocked the CB1 receptor-evoked activation of PKB, pointing to the sequential involvement of a Gi/Go protein and phosphoinositide 3'-kinase. The functionality of the cannabinoid-induced stimulation of PKB was proved by the increased phosphorylation of glycogen synthase kinase-3 serine 21 observed in cannabinoid-**treated** cells and its prevention by SR 141716 and wortmannin. Cannabinoids activated PKB in the human **astrocytoma** cell line U373 MG, which expresses the CB1 receptor, but not in the human promyelocytic cell line HL-60, which expresses the CB2 receptor. Data indicate that activation of PKB may be responsible for some of the effects of cannabinoids in cells expressing the CB1 receptor.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:555508 HCAPLUS
DOCUMENT NUMBER: 131:347583
TITLE: Perinatal exposure to substances present in plants and other compounds causes the development of diseases during the adult age, by the mechanism of imprinting
AUTHOR(S): Tchernitchin, A. N.; Tchernitchin, N. N.
CORPORATE SOURCE: Laboratory of Experimental Endocrinology and Environmental Pathology LEEPA, Center for Research on Environment and Biomedicine CIMAB Institute of Biomedical Sciences ICBM, University of Chile Medical School, Santiago, Chile
SOURCE: Acta Horticulturae (**1999**), 501(Second World Congress on Medicinal and Aromatic Plants for Human Welfare), 19-29
CODEN: AHORA2; ISSN: 0567-7572
PUBLISHER: International Society for Horticultural Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with many refs. Since the first reports linking the development of clear cell cervicovaginal **adenocarcinoma** in young women with diethylstilbestrol **treatment** of their mothers during pregnancy, it became clear that prenatal or neonatal exposure to several substances may generate irreversible alterations, that can be detected later in life. Current evidence suggests that these substances induce, by the mechanism of imprinting, persistent alterations of the differentiation of several cell-types, which, in turn, are involved in the development of various diseases during the adult age. Among plant agents inducing imprinting mechanisms, the best known are phytoestrogens, caffeine, nicotine, fluoride, **tetrahydrocannabinol**, cocaine, opiate alkaloids, digoxin, Valeriana active agents and antithyroid compds. Medicinal plants and agriculture derived food may be addnl. contaminated by polluting agents known to induce imprinting mechanisms, such as lead, pesticides, nitrates and nitrites. Perinatal exposure to phytoestrogens may cause in adults female infertility, immune deficiency, increase in the incidence of infectious and autoimmune diseases and neurobehavioral alterations. Perinatal exposure to caffeine induces neurobehavioral changes, inhibits the differentiation of fetal Leydig cells and decreases the synthesis of fetal testosterone, which in turn alters subsequent development. Nicotine causes biochem. changes in brain, kidney and heart and, in rats, interferes with male sexual activity. Fluoride, present in tea, causes specific neurobehavioral deficit. Perinatal exposure to cocaine, **tetrahydrocannabinol** or opiate alkaloids causes in adults biochem. changes in brain and irreversible neurobehavioral impairment. Antithyroid compds. present in several Cruciferae food products, as well as in Araucaria araucana seeds, induces hypothyroidism in pregnant women, which causes in their offspring irreversible changes in levels and action of thyroid hormones. There exist a wide spectrum of pharmaceutical agents in medicinal plants that had not been investigated for their potential to induce the imprinting mechanism. The discovery of imprinting-mediated perinatal exposure delayed effects should incentive research in this new field of phytopharmacol.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:593494 HCAPLUS
DOCUMENT NUMBER: 129:298319
TITLE: Regulation of δ opioid receptors by Δ9-**tetrahydrocannabinol** in NG108-15 hybrid cells
AUTHOR(S): Di Toro, Rosanna; Campana, Gabriele; Sciarretta, Vittorio; Murari, Giovanna; Spampinato, Santi
CORPORATE SOURCE: Department of Pharmacology, University of Bologna, Bologna, 40126, Italy
SOURCE: Life Sciences (**1998**), 63(14), PL197-PL204
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study we employed the **neuroblastoma** x glioma NG 108-15 cell line as a model for investigating the effects of long-term activation of cannabinoid receptors on δ opioid receptor desensitization, down-regulation and gene expression. Exposure of NG 108-15 cells to (-)-Δ9- **tetrahydrocannabinol** (Δ9-THC) reduced opioid receptor binding, evaluated in intact cells, by ≈ 40 -45% in cells exposed for 24 h to 50 and 100 nM Δ9-THC and by ≈ 25% in cells exposed to 10 nM Δ9-THC. Lower doses of Δ9-THC (0.1 and 1 nM) or a shorter exposure time to the cannabinoid (6 h) were not

effective. Down-regulation of δ opioid receptors was not observed in cells exposed for 24 h to pertussis toxin (PTX) and then **treated** for 24 h with 100 nM Δ9-THC. In cells that were exposed for 24 h to the cannabinoid, the ability of Δ9-THC and of the δ opioid receptor agonist [D-Ser2, Leu5, Thr6]enkephalin to inhibit forskolin-stimulated cAMP accumulation was significantly attenuated. Prolonged exposure of NG 108-15 cells to 100 nM Δ9-THC produced a significant elevation of steady-state levels of δ opioid receptor mRNA. This effect was not observed in cells **pretreated** with PTX. The selective cannabinoid receptor antagonist SR 141716A blocked the effects elicited by Δ9-THC on δ opioid receptor desensitization, down-regulation and gene expression; thus indicating that these are mediated via activation of cannabinoid receptors. These data demonstrate the existence, in NG 108-15 cells, of a complex cross-talk between the cannabinoid and opioid receptors on prolonged exposure to Δ9-THC triggered by changes in signaling through Gi and/or G0-coupled receptors.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:239514 HCAPLUS
DOCUMENT NUMBER: 126:312129
TITLE: Receptor mediation in cannabinoid stimulated arachidonic acid mobilization and anandamide synthesis
AUTHOR(S): Hunter, Sheila A.; Burstein, Sumner H.
CORPORATE SOURCE: Dep. Biochem., Univ. Massachusetts Med. Sch., Worcester, MA, 01655-0103, USA
SOURCE: Life Sciences (**1997**), 60(18), 1563-1573
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous reports have suggested that increased synthesis of eicosanoids is a significant effect of cannabinoids in several models including the human. To address the question of receptor mediation in this process we have carried out expts. using oligonucleotides that are antisense to the CB1 and to the CB2 receptors. We have synthesized sense, antisense and random oligonucleotide probes to test for receptor involvement in THC stimulation of arachidonic acid release in three cell lines of both central and peripheral origin. **Treatment** of N18 mouse **neuroblastoma** cells with the CB1 antisense probe, at two concns., resulted in a dramatic decrease of THC stimulated arachidonate release while **treatment** with antisense CB2 was less effective. Synthesis of the novel eicosanoid, anandamide, was also reduced by antisense CB1 but not by antisense CB2. Western blot anal. indicated a decreased level of CB1 in CB1 antisense **treated** cells. The CB1 antagonist, SR141716A, was effective in reducing the THC elevated levels of free arachidonate in these cells in agreement with the antisense data. In the macrophage line, RAW 264.7, we found that while the sense, the random and the CB1 antisense oligonucleotides were ineffective, the CB2 antisense probe gave significant redns. of the THC induced response. The CB2 probe was also effective in reducing the release of arachidonate in WI-38 human lung fibroblasts. These findings support the idea of a receptor mediated process for cannabinoid stimulation of eicosanoid synthesis.

L26 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:711866 HCAPLUS

DOCUMENT NUMBER: 126:1046
TITLE: Tau protein for delta-9 **tetrahydrocannabinol** in a human **neuroblastoma** cell line
AUTHOR(S): Lew, G. M.
CORPORATE SOURCE: College Human Medicine, Michigan State Univ., East Lansing, MI, 48824, USA
SOURCE: General Pharmacology (**1996**), 27(7), 1141-1143
CODEN: GEPHDP; ISSN: 0306-3623
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1. A human **neuroblastoma** cell line, SH-SY5Y, was used to determine the effects of delta-9-**tetrahydrocannabinol** (THC) on microtubule-associated tau protein. 2. After 48-h **treatment**, THC (10-9 M) decreased 50 kD tau protein in the cytoplasmic (supernatant) fraction, and in the membrane (pellet) fraction the drug (10-7 M) also decreased 50 kD tau protein. 3. This reduction in tau protein was accompanied by a 27% reduction ($P<0.05$) in the membrane (pellet) total protein after (10-7 M) THC and a 28% increase ($P<0.02$) in cytoplasmic (supernatant) total protein after 10-9 M THC.

L26 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:578313 HCAPLUS
DOCUMENT NUMBER: 125:266063
TITLE: Hormonal **treatment** in advanced non-small cell lung cancer: Fact or fiction?
AUTHOR(S): Vansteenkiste, J. F.; Simons, J. P.; Wouters, E. F.; Demedts, M. G.
CORPORATE SOURCE: University Hospital Gasthuisberg, Catholic University, Louvain, B-3000, Belg.
SOURCE: European Respiratory Journal (**1996**), 9(8), 1707-1712
CODEN: ERJOEI; ISSN: 0903-1936
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 48 refs. In patients with advanced non-small cell lung cancer, cachexia is an important cause of morbidity and mortality. The pathogenic mechanism of this finding, usually referred to as "cancer anorexia and cachexia syndrome" (CACS), is complex and far from completely understood, but a disturbed equilibrium between possible food intake and metabolic needs seems to be fundamental. The literature data on the **treatment** options in advanced non-small cell lung cancer (NSCLC) with cachexia are reviewed. Based on the clin. studies on cancer cachexia, some recommendations for the **therapeutic** approach of this disorder in patients with advanced NSCLC can be given. Metoclopramide is easily administered, can alleviate gastric disturbances, but probably does not correct the catabolic spiral of CACS. There are not enough data to advise the use of parenteral nutritional support, hydrazine, cyproheptadine, **tetrahydrocannabinol** or nandrolone decanoate. Corticosteroids are useful in addnl. analgesia and fast palliation of very weak and debilitated patients in the final episode of their disease. Recent data in non-small cell lung cancer patients are in favor of the use of high-dose progestagens to **improve** both appetite and weight

L26 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:983441 HCAPLUS

DOCUMENT NUMBER: 124:76301
TITLE: Activation of mitogen-activated protein kinases by stimulation of the central cannabinoid receptor CB1
AUTHOR(S): Bouaboula, Monsif; Poinot-Chazel, Caroline; Bourrie, Bernard; Canat, Xavier; Calandra, Bernard; Rinaldi-Carmona, Murielle; Le Fur, Gerard; Casellas, Pierre
CORPORATE SOURCE: Sanofi Recherche, Dep. Immunopharmacology, Montpellier, 34184, Fr.
SOURCE: Biochemical Journal (**1995**), 312(2), 637-41
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The G-protein-coupled central cannabinoid receptor (CB1) has been shown to be functionally associated with several biol. responses including inhibition of adenylate cyclase, modulation of ion channels and induction of the immediate-early gene Krox-24. Using stably transfected Chinese Hamster Ovary cells expressing human CB1 we show here that cannabinoid **treatment** induces both phosphorylation and activation of mitogen-activated protein (MAP) kinases, and that these effects are inhibited by SR 141716A, a selective CB1 antagonist. The two p42 and p44 kDa MAP kinases are activated in a time- and dose-dependent manner. The rank order of potency for the activation of MAP kinases with various cannabinoid agonists is CP-55940 > Δ9- **tetrahydrocannabinol** > WIN 55212.2, in agreement with the pharmacol. profile of CB1. The activation of MAP kinases is blocked by pertussis toxin but not by **treatment** with hydrolysis-resistant cAMP analogs. This suggests that the signal transduction pathway between CB1 and MAP kinases involves a pertussis-toxin-sensitive GTP-binding protein and is independent of cAMP metabolism This coupling of CB1 subtype and mitogenic signal pathway, also observed in the human **astrocytoma** cell line U373 MG, may explain the mechanism of action underlying cannabinoid-induced Krox-24 induction.

L26 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:367242 HCAPLUS
DOCUMENT NUMBER: 122:151262
TITLE: Low doses of anandamides inhibit pharmacological effects of Δ9- **tetrahydrocannabinol**
AUTHOR(S): Fride, E.; Barg, J.; Levy, R.; Saya, D.; Heldman, E.; Mechoulam, R.; Vogel, Z.
CORPORATE SOURCE: Medical Faculty, Hebrew University Jerusalem, Jerusalem, 91120, Israel
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1995**), 272(2), 699-707
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been shown previously that the endogenous cannabinoid receptor ligand arachidonylethanolamide (anandamide 20:4, n-6) induces in vivo and in vitro effects typical of a cannabinoid partial agonist. We now report that the synthetic docosahexaenylethanolamide (anandamide 22:6, n-3) shows similar activities. In addition we show that these two anandamides, under certain exptl. conditions, antagonize the effects of Δ9-THC both in vivo and in vitro. Thus a significant decrease in the potency of Δ9-THC-induced inhibition of adenylate cyclase was observed in N18TG2 **neuroblastoma** cells that were **pretreated** with low concns. of anandamides. At these low concns. of anandamides had no effect

when applied alone. In vivo, Sabra or ICR mice were subjected to a tetrad of tests, designed to detect cannabinoid-induced effects. Mice **pretreated** (i.p.) with 10 mg/kg of Δ9-THC received injections with anandamides. Only low doses (0.0001-0.1 mg/kg) of the anandamides, which had no effects when administered alone, partially or fully inhibited the THC-induced effects. These findings suggest that the inhibition of Δ9-THC-induced effects by low doses of anandamides may be due to their partial agonistic effects. It is possible that low doses of the anandamides are capable of activating a Gs protein mediated signaling pathway, or may cause an allosteric modulation of the cannabinoid receptor.

L26 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:473911 HCAPLUS
DOCUMENT NUMBER: 121:73911
TITLE: Inhibitors of arachidonic acid metabolites for preventing neurological damage, and screening method for neuroprotectants
INVENTOR(S): Bernton, Edward W.; Jett, Marti; Gendelman, Howard
PATENT ASSIGNEE(S): United States Department of the Army, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9412667	A1	19940609	WO 1993-US11542	19931129 <--

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1992-982656 A 19921127 <--
US 1993-61970 A 19930902 <--

AB A method is provided for **treating** encephalitis or encephalopathy secondary to CNS infection by administration of **therapeutically** effective amts. of compns. which inhibit the release of platelet activation factor and/or arachidonate metabolites. Compns. are disclosed containing e.g. 11-nor-**.DELTA.8-tetrahydrocannabinol**-9-carboxylic acid or nordihydroguaiaretic acid. Also provided are methods for screening for compds. that have neuroprotective activity; the methods comprise infecting monocytes or lymphocytes with an infectious organism known to cause neural damage, adding the resulting infected culture to a culture of astrocyte cells, adding a test compound, allowing sufficient time to pass for the production of TNF-alpha, withdrawing aliquots from the supernatant of the culture, adding the aliquots to cultures of neural cells and identifying which supernatants impart a neuroprotective effect.

L26 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:420323 HCAPLUS
DOCUMENT NUMBER: 117:20323
TITLE: Cannabinoids inhibit N-type calcium channels in **neuroblastoma**-glioma cells
AUTHOR(S): Mackie, Ken; Hille, Bertil
CORPORATE SOURCE: Sch. Med., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1992**), 89(9), 3825-9

CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The psychoactive properties of Cannabis sativa and its major biol. active constituent, Δ9- **tetrahydrocannabinol**, have been known for years. The recent identification and cloning of a specific cannabinoid receptor suggest that cannabinoids mimic endogenous compds. affecting neural signals for mood, memory, movement, and pain. Using whole-cell voltage clamp and the cannabinomimetic aminoalkylindole WIN 55,212-2, it has been found that cannabinoid receptor activation reduces the amplitude of voltage-gated calcium currents in the **neuroblastoma**-glioma cell line NG108-15. The inhibition is potent, being half-maximal at less than 10 nM, and reversible. The inactive enantiomer, WIN 55,212-3, does not reduce calcium currents even at 1 μM. Of the several types of calcium currents in NG108-15 cells, cannabinoids predominantly inhibit an ω-conotoxin-sensitive, high-voltage-activated calcium current. Inhibition was blocked by incubation with pertussis toxin but was not altered by prior **treatment** with hydrolysis-resistant cAMP analogs together with a phosphodiesterase inhibitor, suggesting that the transduction pathway between the cannabinoid receptor and calcium channel involves a pertussis toxin-sensitive GTP-binding protein and is independent of cAMP metabolism However, the development of inhibition is considerably slower than a pharmacol. similar pathway used by an α2-adrenergic receptor in these cells. Results suggest that inhibition of N-type calcium channels, which could decrease excitability and neurotransmitter release, may underlie some of the psychoactive effects of cannabinoids.

L26 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:526814 HCAPLUS
DOCUMENT NUMBER: 115:126814
TITLE: Marijuana decreases macrophage antiviral and antitumor activities
AUTHOR(S): Cabral, G. A.; Vasquez, R.
CORPORATE SOURCE: Med. Coll. Virginia, VCU, Richmond, VA, 23298-0678, USA
SOURCE: Advances in the Biosciences (Oxford) (**1991**), 80(Physiopathol. Illicit Drugs: Cannabis, Cocaine, Opiates), 93-105
CODEN: AVBIB9; ISSN: 0065-3446
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Delta-9-**tetrahydrocannabinol** (THC), the major psychoactive component of marijuana, was shown to decrease macrophage functional competence against tumor cells and virus-infected cells. Peritoneal macrophages of :(B6C3)F1 mice receiving Propionibacterium acnes as a macrophage "activator" and **treated** with THC (50 mg/kg and 100 mg/kg) exhibited a dose-related decrease in effector cell:target cell contact-dependent tumoricidal activity against rat B103 **neuroblastoma** cells. Macrophage-like cells of the lines J774A.1, P388D1, or RAW264.7 exposed in vitro to THC exhibited decreased extrinsic antiviral activity to herpes simplex virus type 2. SEM demonstrated that THC administered in vivo or in vitro did not prevent P. acnes macrophages or the macrophage-like cells from attaching to tumor or virus-infected target cells. However, the drug inhibited protein expression by macrophages in response to stimuli such as P. acnes in vivo and bacterial lipopolysaccharide in vitro. These results suggest that THC inhibits "full" activation of macrophages since tumoricidal and antiviral activities are characteristic features of macrophage "full" activation.

Furthermore, since contact-dependent tumoricidal and extrinsic antiviral activities are two-step processes in which effector cell:target cell conjugation is followed by delivery of effector mols., these results indicate that the cannabinoid acted at the level of inhibition of effector mol. expression.

L26 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:48399 HCAPLUS
DOCUMENT NUMBER: 112:48399
TITLE: The effect of marijuana smoke exposure on murine **sarcoma** 180 survival in Fisher rats
AUTHOR(S): Watson, E. Sue
CORPORATE SOURCE: Res. Inst. Pharm. Sci., Sch. Pharm., University, MS, 38677, USA
SOURCE: Immunopharmacology and Immunotoxicology (**1989**), 11(2-3), 211-22
CODEN: IITOEF; ISSN: 0892-3973
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fisher rats were **treated** for 28 or 60 days to multiple exposures to the smoke of marijuana or marijuana placebo cigarettes. Primary, secondary and in some instances tertiary tumor implants were performed. Murine **sarcoma** 180 tumor cells (7.5 + 107) were implicated s.c. on day 1, 14 and 28 following initiation of smoke exposure (28 day studies) or on day 1, 14 after cessation of smoke exposure (60 day studies). Tumor areas were measured on alternate days beginning on the second or third day after implantation for 13 or 14 days. Exposure to both marijuana and placebo smoke for 28 days (6, 9 and 18 cigarettes per day) resulted in suppressed growth of secondary and tertiary implants. Administration of Δ9- **tetrahydrocannabinol** (50 mg/kg, i.p., 20 days) failed to suppress the growth of primary and secondary tumors. This suggests that noncannabinoid constituents of the smoke may contribute to the suppression of tumor growth. Exposure of rats to 9, but not 4 or 6, marijuana or placebo cigarettes per day for 60 days suppressed the growth of primary but not secondary tumors. Thus, the effects of smoke exposure appear to be lose by 2 wk after cessation of **treatment.** The possible existence of a non-cannabinoid immunostimulant in the smoke is discussed.

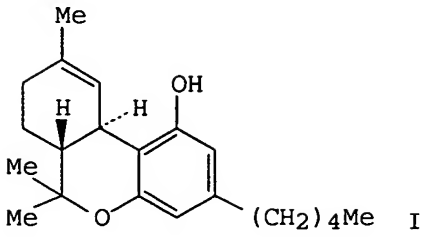
L26 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:198239 HCAPLUS
DOCUMENT NUMBER: 108:198239
TITLE: Regulation of adenylate cyclase by chronic exposure to cannabimimetic drugs
AUTHOR(S): Dill, Jill A.; Howlett, Allyn C.
CORPORATE SOURCE: Sch. Med., St. Louis Univ., St. Louis, MO, 63104, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1988**), 244(3), 1157-63
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Short-term exposure to either Δ9-THC or the more potent nantradol analog, desacetyllevonantradol (DALN), at ≤100 μM did not compromise the plating efficiency of **neuroblastoma** cells. Cells that were exposed to 1 μM Δ9-THC (maximally effective for inhibiting cAMP production) for 24 h in a serum-free medium were shown to accumulate the drug but not to metabolize it. Exposure to 10 μM Δ9-THC or DALN for up to 48 h failed to affect cell growth rate or protein content per cell. The gross morphol. of cannabinoid-

treated cells was not altered at the light or the electron microscope level. The cellular organelles and membranes appeared intact, with no remarkable differences from control cells. The inhibition of cAMP accumulation in response to cannabimimetic drugs was diminished in cells **treated** with Δ9-THC or DALN for 24 h. This desensitization was homologous because both Δ9-THC and DALN responses were attenuated after exposure to either cannabimimetic drug. In contrast, the inhibition of cAMP accumulation in response to carbachol via the muscarinic receptor was unaltered by previous exposure of the cells to cannabimimetic agents. For DALN, the desensitization could be observed as early as 4 h and was dose-dependent. These studies demonstrate that desensitization of the cannabimimetic regulation of adenylate cyclase can occur in the absence of cytotoxicity.

L26 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:629021 HCAPLUS
DOCUMENT NUMBER: 107:229021
TITLE: Interaction of delta-9-**tetrahydrocannabinol** with rat B103 **neuroblastoma** cells
AUTHOR(S): Cabral, Guy A.; McNerney, Peter J.; Mishkin, Eric M.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
SOURCE: Archives of Toxicology (**1987**), 60(6), 438-49
CODEN: ARTODN; ISSN: 0340-5761
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of Δ9- **tetrahydrocannabinol** (Δ9-THC) on the growth kinetics and morphol. of rat B103 **neuroblastoma** cells was assessed. Δ9-THC in doses ranging from 10-4 to 10-7 M inhibited cellular growth in a dose-dependent fashion as evidenced by delay in doubling time, decrease in saturation d., and decrease in efficiency of plating. The inhibition in cellular growth was paralleled by dose-related alterations in cell morphol. Modifications included rounding of cells, retraction of neurites, blebbing of the cell surface, and exfoliation of the plasma membrane. Cytoplasmic alterations included distension of the endoplasmic reticulum, Golgi apparatus, and perinuclear space, and macrovacuolization. Intracytoplasmic laminated inclusions and vesicular clusters were suggestive of membrane repair in drug-**treated** cells. These morphol. changes were accompanied by cytoskeletal rearrangement in the absence of significant alteration in the concentration of total cytoskeletal protein. Autoradiog. examination of the intracellular fate of 3H-Δ9-THC demonstrated that the drug was confined to the cytoplasmic compartment and often associated with macrovacuoles. These results suggest that Δ9-THC interacts with cellular membranes, thereby altering **neuroblastoma** cell growth and behavior. The results are discussed in relation to drug interactions and herpes simplex virus 2 infection.

L26 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:448191 HCAPLUS
DOCUMENT NUMBER: 101:48191
TITLE: Influence of Δ9- **tetrahydrocannabinol** on expression of histone and ribosomal genes in normal and transformed human cells
AUTHOR(S): Green, Linda G.; Stein, Janet L.; Stein, Gary S.
CORPORATE SOURCE: Coll. Med., Univ. Florida, Gainesville, FL, 32610, USA
SOURCE: Biochemical Pharmacology (**1984**), 33(7), 1033-40
CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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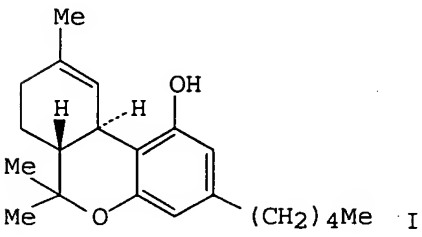
AB The influence of Δ9-THC (I) [1972-08-3] on the cellular levels of histone mRNAs and rRNAs was examined in several normal and transformed human cell lines-HeLa S3 cells, WI-38 human diploid fibroblasts, SV40-transformed WI-38 cells, and A549 lung **carcinoma** cells. **Treatment** with Δ9-THC (10-40 μM) for 10 h resulted in a concentration-dependent decrease in the representation of H2A, H2B, H3 and H4 histone mRNAs without a significant inhibitory effect on the levels of rRNAs. The cannabinoid-mediated inhibitory effect on histone gene expression was less evident in cells with active drug-metabolizing systems.

L26 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:69581 HCAPLUS
DOCUMENT NUMBER: 92:69581
TITLE: Long term effects of Δ9-**tetrahydrocannabinol** in mice
AUTHOR(S): Szepsenwol, J.; Fletcher, J.; Murison, G. L.; Toro-Goyco, E.
CORPORATE SOURCE: Dep. Biol. Sci., Florida Int. Univ., Miami, FL, USA
SOURCE: Advances in the Biosciences (Oxford) (**1979**), Volume Date 1978, 22-23(Marihuana: Biol. Eff.), 359-70
CODEN: AVBIB9; ISSN: 0065-3446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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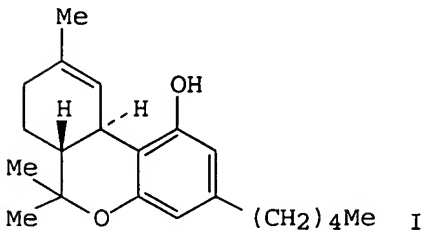
AB Δ9- **Tetrahydrocannabinol** (I) [1972-08-3] (20 μg/0.05 mL sesame oil/wk, s.c.) unlike estrogen did not interfere with the normal development or reproduction of C57 B1/6 and BALB/c mice. It caused, however, a high mortality rate among the offspring. This was particularly high

among the C57 B1/6 strain and was apparently due to an inhibitory effect upon the milk secretion by the mammary gland, since newborn C57 B1/6 mice which had no milk in their stomachs the day after birth survived and developed normally when foster nursed by lactating BALB/c females. Four of 200 BALB/c I-**treated** mice developed **fibrosarcomas** at the point of injection of the drug. Of 46 C57 B1/6 I-**treated** mice, 1 developed a mammary **adenocarcinoma**.. Of the 32 BALB/c females receiving injections of sesame oil, 8 developed mammary **adenocarcinomas**. Thus, it is thought that sesame oil had an estrogenic effect; it causes mammary carcinogenesis by increasing the production of LH and LTH. I appears to have an antiestrogenic effect, causing a decrease in LH and LTH, which is the cause of defective secretion of milk by the mammary glands and the high mortality of the offspring, particularly of the C57 B1/6 mice. In addition, I appears to have a carcinogenic effect by stimulating development of mesenchymal tumors. Its effect upon parenchymal tumors may be inhibitory.

L26 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:164045 HCAPLUS
DOCUMENT NUMBER: 88:164045
TITLE: In vivo effects of cannabinoids on macromolecular biosynthesis in Lewis lung **carcinomas**
AUTHOR(S): Friedman, Marvin A.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, USA
SOURCE: Cancer Biochemistry Biophysics (**1977**), 2(2), 51-4
CODEN: CABCD4; ISSN: 0305-7232
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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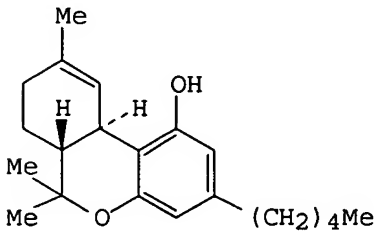
AB The effects of Δ9-THC (I) [1972-08-3]Δ8-THC [**5957-75-5**], and **cannabidiol** [**13956-29-1**] on tumor macromol. biosynthesis in mice bearing Lewis lung **carcinomas** were studied. The drugs inhibited thymidine-3H incorporation into DNA acutely, but did not inhibit leucine uptake into tumor protein. At 24 h after **treatment**, cannabinoids did not inhibit thymidine-3H incorporation into DNA, leucine-3H uptake into protein or cytidine-3H into RNA.

L26 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:487170 HCAPLUS
DOCUMENT NUMBER: 85:87170
TITLE: Effects of Δ9- **tetrahydrocannabinol** in Lewis lung **adenocarcinoma** cells in tissue culture

AUTHOR(S): White, A. C.; Munson, J. A.; Munson, A. E.; Carchman, R. A.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, USA
SOURCE: Journal of the National Cancer Institute (1940-1978) (**1976**), 56(3), 655-8
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB There was a dose-related decrease in DNA synthesis in transformed cell cultures **treated** with Δ9- **tetrahydrocannabinol** (I) [1972-08-3]. The decrease, observed over a 4-hour period, was not accompanied by a change in the radioactive precursor pool as compared to that of control cultures. The distribution of labeled products clearly differed from that observed after **treatment** with cytosine arabinoside [147-94-4]. I inhibited DNA synthesis at some point beyond the uptake of 3H-thymidine.

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=> d ibib abs l26 1-26

L26 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60544 HCAPLUS
DOCUMENT NUMBER: 140:144682
TITLE: Molecular antigen arrays comprising AP205 virus-like particle and antigen for prevention and **treatment** of cancer, drug addiction, poisoning, infection, and allergy
INVENTOR(S): Bachmann, Martin F.; Tissot, Alain; Pumpens, Paul; Cielens, Indulis; Renhofa, Regina
PATENT ASSIGNEE(S): Cytos Biotechnology AG, Switz.
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007538	A2	20040122	WO 2003-EP7572	20030714 <--
WO 2004007538	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2489410	AA	20040122	CA 2003-2489410	20030714 <--
US 2004076611	A1	20040422	US 2003-617876	20030714 <--
EP 1532167	A2	20050525	EP 2003-763829	20030714 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012935	A	20050621	BR 2003-12935	20030714 <--
PRIORITY APPLN. INFO.:			US 2002-396126P P	20020717 <--
			WO 2003-EP7572 W	20030714 <--

AB The present invention provides a composition comprising an AP205 virus like particle (VLP) and an antigen. The invention also provides a process for producing an antigen or antigenic determinant bound to AP205 VLP. AP205 VLP bound to an antigen is useful in the production of compns. for inducing immune responses that are useful for the prevention or **treatment** of diseases, disorders or conditions including infectious diseases, allergies, cancer, drug addiction, poisoning and to efficiently induce self-specific immune responses, in particular antibody responses.

L26 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472379 HCAPLUS
DOCUMENT NUMBER: 139:30794
TITLE: Method for the **treatment** of neoplasia
INVENTOR(S): Nagarkatti, Mitzi; Nagarkatti, Prakash; McKallip, Robert; Lombard, Catherine; Ryu, Seongho

PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003049727	A1	20030619	WO 2002-US39310		20021209 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2468794	AA	20030619	CA 2002-2468794		20021209 <--
EP 1461027	A1	20040929	EP 2002-804754		20021209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005516004	T2	20050602	JP 2003-550776		20021209 <--
US 2004259936	A1	20041223	US 2004-497911		20040813 <--
PRIORITY APPLN. INFO.:			US 2001-336732P	P	20011207 <--
			WO 2002-US39310	W	20021209 <--

AB Method is disclosed for the **treatment** of patients with abnormality in cells of the immune system comprising administration of a **therapeutically** ED of a compound having CB2 cannabinoid receptor activity. The abnormality is particularly a malignancy such as a leukemia or lymphoma.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242184 HCAPLUS
DOCUMENT NUMBER: 138:285995
TITLE: Packaging of immunostimulatory substances and antigens into virus-like particles for use as vaccines against cancer, autoimmune disease, allergy and viral infection
INVENTOR(S): Maurer, Patrick; Tissot, Alain; Schwarz, Katrin; Meijerink, Edwin; Lipowsky, Gerad; Pumpens, Paul; Cielens, Indulis; Renhofa, Regina; Bachmann, Martin F.; Storni, Tazio
PATENT ASSIGNEE(S): Cytos Biotechnology A.-G., Switz.
SOURCE: PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024481	A2	20030327	WO 2002-IB4132	20020916 <--

WO 2003024481 A3 20040603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2492826 AA 20030327 CA 2002-2492826 20020916 <--
US 2003099668 A1 20030529 US 2002-244065 20020916 <--
EP 1450856 A2 20040901 EP 2002-777600 20020916 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
JP 2005517632 T2 20050616 JP 2003-528575 20020916 <--
PRIORITY APPLN. INFO.: US 2001-318994P P 20010914 <--
US 2002-374145P P 20020422 <--
WO 2002-IB4132 W 20020916 <--

AB The invention relates to the finding that virus-like particles (VLPs) can be loaded with immunostimulatory substances, in particular with DNA oligonucleotides containing non-methylated C and G (CpGs). Such CpG-VLPs are dramatically more immunogenic than their CpG-free counterparts and induce enhanced B and T cell responses. The immune response against antigens optionally coupled, fused or attached otherwise to the VLPs is similarly enhanced as the immune response against the VLP itself. In addition, the T cell responses against both the VLPs and antigens are especially directed to the Th1 type. Antigens attached to CpG-loaded VLPs may therefore be ideal vaccines for prophylactic or **therapeutic** vaccination against allergies, tumors and other self-mols. and chronic viral diseases.

L26 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242183 HCAPLUS
DOCUMENT NUMBER: 138:270293
TITLE: Vaccine compositions comprising anti-CD4 antibody or immunostimulatory nucleic acid and antigen-coupled virus-like particles for enhancement of immune responses
INVENTOR(S): Bachmann, Martin F.; Storni, Tazio; Lechner, Franziska
PATENT ASSIGNEE(S): Cytos Biotechnology A.-G., Switz.
SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024480	A2	20030327	WO 2002-IB4252	20020916 <--
WO 2003024480	A3	20031030		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2492823	AA	20030327	CA 2002-2492823		20020916 <--
US 2003091593	A1	20030515	US 2002-243739		20020916 <--
EP 1425040	A2	20040609	EP 2002-783338		20020916 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005507388	T2	20050317	JP 2003-528574		20020916 <--
PRIORITY APPLN. INFO.:			US 2001-318967P	P	20010914 <--
			WO 2002-IB4252	W	20020916 <--

AB The invention relates to the finding that stimulation of antigen presenting cell (APC) activation using substances such as anti-CD40 antibodies or DNA oligomers rich in non-methylated C and G (CpGs) can dramatically enhance the specific T cell response obtained after vaccination with recombinant virus like particles (VLPs) coupled, fused or otherwise attached to antigens. While vaccination with recombinant VLPs fused to a cytotoxic T cell (CTL) epitope of lymphocytic choriomeningitis virus induced low levels cytolytic activity only and did not induce efficient anti-viral protection, VLPs injected together with anti-CD40 antibodies or CpGs induced strong CTL activity and full anti-viral protection for **treating** tumors and chronic viral diseases. Thus, stimulation of APC-activation through antigen presenting cell activators such as anti-CD40 antibodies or CpGs can exhibit a potent adjuvant effect for vaccination with VLPs coupled, fused or attached otherwise to antigens.

L26 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2001:322837 HCAPLUS
DOCUMENT NUMBER:	135:132395
TITLE:	Characterization of palmitoylethanolamide transport in mouse Neuro-2a **neuroblastoma** and rat RBL-2H3 basophilic leukaemia cells: comparison with anandamide
AUTHOR(S):	Jacobsson, Stig O. P.; Fowler, Christopher J.
CORPORATE SOURCE:	Department of Pharmacology and Clinical Neuroscience, Department of Odontology, Umea University, Umea, SE-901 87, Swed.
SOURCE:	British Journal of Pharmacology (**2001**), 132(8), 1743-1754 CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The endogenous cannabinoid receptor agonist anandamide (AEA) and the related compound palmitoylethanolamide (PEA) are inactivated by transport into cells followed by metabolism by fatty acid amide hydrolase (FAAH). The cellular uptake of AEA has been characterized in detail, whereas less is known about the properties of the PEA uptake, in particular in neuronal cells. In the present study, the pharmacol. and functional properties of PEA and AEA uptake have been investigated in mouse Neuro-2a **neuroblastoma** and, for comparison, in rat RBL-2H3 basophilic leukemia cells. Saturable uptake of PEA and AEA into both cell lines were demonstrated with apparent KM values of 28 μM (PEA) and 10 μM (AEA) in Neuro-2a cells, and 30 μM (PEA) and 9.3 μM (AEA) in RBL-2H3 cells. Both PEA and AEA uptake showed temperature-dependence but only the AEA uptake was sensitive to **treatment** with Pronase and phenylmethylsulfonyl fluoride. The AEA uptake was inhibited by AM404, 2-arachidonoylglycerol (2-AG), R1- and S1-methanandamide, arachidonic acid

and olvanil with similar potencies for the two cell types. PEA, up to a concentration of 100 μM, did not affect AEA uptake in either cell line. AEA, 2-AG, arachidonic acid, R1-methanandamide, Δ9-THC, and **cannabidiol** inhibited PEA transport in both cell lines. The non-steroidal anti-inflammatory drug indomethacin inhibited the AEA uptake but had very weak effects on the uptake of PEA. From these data, it can be concluded that PEA is transported in to cells both by passive diffusion and by a facilitated transport that is pharmacol. distinguishable from AEA uptake.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:688060 HCAPLUS
DOCUMENT NUMBER: 133:247279
TITLE: Alkyl resorcinols, **cannabinols**, **cannabidiols**, and cannabigerols for **treatment** of diseases associated with immune dysfunction, viral infections, and neoplasms
INVENTOR(S): Travis, Craig R.
PATENT ASSIGNEE(S): Immugen Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2000056303	A2	20000928	WO 2000-US7629		20000322	<--
WO 2000056303	A3	20020124				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
CA 2367262	AA	20000928	CA 2000-2367262		20000322	<--
AU 2000039107	A5	20001009	AU 2000-39107		20000322	<--
BR 2000009200	A	20011226	BR 2000-9200		20000322	<--
EP 1189603	A2	20020327	EP 2000-918266		20000322	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
JP 2002539246	T2	20021119	JP 2000-606208		20000322	<--
ZA 2001007773	A	20030422	ZA 2001-7773		20010920	<--
PRIORITY APPLN. INFO.:			US 1999-125674P	P	19990322	<--
			US 1999-151595P	P	19990830	<--
			WO 2000-US7629	W	20000322	<--

AB The invention provides a method, compds., and compns. for **treating** a disease associated with immune dysfunction. A pharmacol.-acceptable composition including ≥1 compound selected from 5-alkyl-resorcinol derivs., **cannabinol** derivs., **cannabidiol** derivs., cannabigerol derivs., and combinations thereof, is administered to a patient under conditions sufficient to attenuate the dysfunction within the immune

system. The invention also provides an antiviral **cannabinol** derivative that can be used in the method. The invention also provides an alkylated resorcinol derivative and a method of using the alkylated resorcinol derivative to attenuate the growth of a neoplasm. The method and compound are useful for **treating** diseases of the immune system, such as HIV disease and neoplastic disorders.

L26 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:493550 HCAPLUS
DOCUMENT NUMBER: 133:101736
TITLE: A reagent system and method for increasing the luminescence of lanthanide(iii) macrocyclic complexes
INVENTOR(S): Leif, Robert C.; Vallarino, Lidia
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042048	A1	20000720	WO 2000-US1211	20000118 <--
W: CA, CH, DE, FI, GB, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2360054	AA	20000720	CA 2000-2360054	20000118 <--
EP 1150985	A1	20011107	EP 2000-905653	20000118 <--
EP 1150985	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6340744	B1	20020122	US 2000-484670	20000118 <--
AT 270298	E	20040715	AT 2000-905653	20000118 <--
US 2002132992	A1	20020919	US 2001-10597	20011206 <--
US 6750005	B2	20040615		
PRIORITY APPLN. INFO.:			US 1999-116316P P	19990119 <--
			US 2000-484670 A1	20000118 <--
			WO 2000-US1211 W	20000118 <--

OTHER SOURCE(S): MARPAT 133:101736
AB Disclosed are a spectrofluorimetrically detectable luminescent composition and processes for enhancing the luminescence of one or more lanthanide-containing macrocycles. The luminescent composition comprises a micelle-producing amount of

at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compound having an emission spectrum peak in the range from 500 to 950 nm, and a luminescence-enhancing amount of at least one energy transfer donor compound of yttrium or a 3-valent lanthanide element having atomic number 59-71, provided that the lanthanide element of said macrocycle compound and the lanthanide element of said energy transfer donor compound are not identical. The addition of gadolinium(III) in the presence of other solutes to both the prototype and the difunctionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patents #5,373,093 and #5,696,240, enhances their luminescence. Similar enhancements of luminescence also results for the mono-functionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patent #5,696,240. The enhanced luminescence afforded by the composition enables the detection and/or quantitation of many analytes in low concns. without the use of expensive, complicated time-gated detection

systems.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:326272 HCAPLUS
DOCUMENT NUMBER: 133:100532
TITLE: Imprinting: perinatal exposures cause the development of diseases during the adult age
AUTHOR(S): Tchernitchin, A. N.; Tchernitchin, Nina N.; Mena, M. A.; Unda, Cristina; Soto, J.
CORPORATE SOURCE: Laboratory of Experimental Endocrinology and Environmental Pathology LEEPA, Institute of Biomedical Sciences ICBM and Environment and Biomedicine Research Center CIMAB, Medical School, University of Chile, Santiago, Chile
SOURCE: Acta Biologica Hungarica (**1999**), 50(4), 425-440
CODEN: ABHUE6; ISSN: 0236-5383
PUBLISHER: Akademiai Kiado
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 121 refs. Since the early reports linking the development of clear cell cervicovaginal **adenocarcinoma** in young women with diethylstilbestrol **treatment** of their mothers during pregnancy, it became clear that perinatal exposure to several substances may induce irreversible alterations, that can be detected later in life. Current evidence suggests that these substances induce, by the mechanism of imprinting, alterations of the differentiation of several cell-types, resulting in the development of disease during the adult age. The most known delayed effects to prenatal exposure to agents displaying hormone action, pollutants, food additives and natural food components, substances of abuse and stress by the mechanism of imprinting are described. Among them, estrogens, androgens, progestins, lead, benzopyrenes, ozone, dioxins, DDT, DDE, methoxychlor, chlordecone, parathion, malathion, polychlorobiphenyls, pyrethroids, paraquat, food additives, normal food constituents, **tetrahydrocannabinol**, cocaine and opiates. It is concluded that perinatal exposure to several agents causes irreversible changes that determine health conditions during adulthood. Several diseases developing during adulthood probably were determined during early stages of life, under the effect of exposure or preferential mother's diet during pregnancy. Regulations to avoid these early exposures may contribute to an important **improvement** of health conditions of humankind.
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:325337 HCAPLUS
DOCUMENT NUMBER: 133:38140
TITLE: The CB1 cannabinoid receptor is coupled to the activation of protein kinase B/Akt
AUTHOR(S): Del Pulgar, Teresa Gomez; Velasco, Guillermo; Guzman, Manuel
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: Biochemical Journal (**2000**), 347(2), 369-373

CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cannabinoids exert most of their effects in the central nervous system through the CB1 cannabinoid receptor. This G-protein-coupled receptor has been shown to be functionally coupled to inhibition of adenylate cyclase, modulation of ion channels and activation of extracellular-signal-regulated kinase. Using Chinese hamster ovary cells stably transfected with the CB1 receptor cDNA we show here that Δ9-**tetrahydrocannabinol** (THC), the major active component of marijuana, induces the activation of protein kinase B/Akt (PKB). This effect of THC was also exerted by the endogenous cannabinoid anandamide and the synthetic cannabinoids CP-55940 and HU-210, and was prevented by the selective CB1 antagonist SR 141716. Pertussis toxin and wortmannin blocked the CB1 receptor-evoked activation of PKB, pointing to the sequential involvement of a Gi/Go protein and phosphoinositide 3'-kinase. The functionality of the cannabinoid-induced stimulation of PKB was proved by the increased phosphorylation of glycogen synthase kinase-3 serine 21 observed in cannabinoid-**treated** cells and its prevention by SR 141716 and wortmannin. Cannabinoids activated PKB in the human **astrocytoma** cell line U373 MG, which expresses the CB1 receptor, but not in the human promyelocytic cell line HL-60, which expresses the CB2 receptor. Data indicate that activation of PKB may be responsible for some of the effects of cannabinoids in cells expressing the CB1 receptor.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:555508 HCAPLUS
DOCUMENT NUMBER: 131:347583
TITLE: Perinatal exposure to substances present in plants and other compounds causes the development of diseases during the adult age, by the mechanism of imprinting
AUTHOR(S): Tchernitchin, A. N.; Tchernitchin, N. N.
CORPORATE SOURCE: Laboratory of Experimental Endocrinology and Environmental Pathology LEEPA, Center for Research on Environment and Biomedicine CIMAB Institute of Biomedical Sciences ICBM, University of Chile Medical School, Santiago, Chile
SOURCE: Acta Horticulturae (**1999**), 501(Second World Congress on Medicinal and Aromatic Plants for Human Welfare), 19-29
CODEN: AHORA2; ISSN: 0567-7572
PUBLISHER: International Society for Horticultural Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with many refs. Since the first reports linking the development of clear cell cervicovaginal **adenocarcinoma** in young women with diethylstilbestrol **treatment** of their mothers during pregnancy, it became clear that prenatal or neonatal exposure to several substances may generate irreversible alterations, that can be detected later in life. Current evidence suggests that these substances induce, by the mechanism of imprinting, persistent alterations of the differentiation of several cell-types, which, in turn, are involved in the development of various diseases during the adult age. Among plant agents inducing imprinting mechanisms, the best known are phytoestrogens, caffeine, nicotine, fluoride, **tetrahydrocannabinol**, cocaine, opiate alkaloids, digoxin, Valeriana active agents and antithyroid compds.

Medicinal plants and agriculture derived food may be addnl. contaminated by polluting agents known to induce imprinting mechanisms, such as lead, pesticides, nitrates and nitrites. Perinatal exposure to phytoestrogens may cause in adults female infertility, immune deficiency, increase in the incidence of infectious and autoimmune diseases and neurobehavioral alterations. Perinatal exposure to caffeine induces neurobehavioral changes, inhibits the differentiation of fetal Leydig cells and decreases the synthesis of fetal testosterone, which in turn alters subsequent development. Nicotine causes biochem. changes in brain, kidney and heart and, in rats, interferes with male sexual activity. Fluoride, present in tea, causes specific neurobehavioral deficit. Perinatal exposure to cocaine, **tetrahydrocannabinol** or opiate alkaloids causes in adults biochem. changes in brain and irreversible neurobehavioral impairment. Antithyroid compds. present in several Cruciferae food products, as well as in Araucaria araucana seeds, induces hypothyroidism in pregnant women, which causes in their offspring irreversible changes in levels and action of thyroid hormones. There exist a wide spectrum of pharmaceutical agents in medicinal plants that had not been investigated for their potential to induce the imprinting mechanism. The discovery of imprinting-mediated perinatal exposure delayed effects should incentive research in this new field of phytopharmacol.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:593494 HCAPLUS
DOCUMENT NUMBER: 129:298319
TITLE: Regulation of δ opioid receptors by Δ9-**tetrahydrocannabinol** in NG108-15 hybrid cells
AUTHOR(S): Di Toro, Rosanna; Campana, Gabriele; Sciarretta, Vittorio; Murari, Giovanna; Spampinato, Santi
CORPORATE SOURCE: Department of Pharmacology, University of Bologna, Bologna, 40126, Italy
SOURCE: Life Sciences (**1998**), 63(14), PL197-PL204
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study we employed the **neuroblastoma** x glioma NG 108-15 cell line as a model for investigating the effects of long-term activation of cannabinoid receptors on δ opioid receptor desensitization, down-regulation and gene expression. Exposure of NG 108-15 cells to (-)-Δ9- **tetrahydrocannabinol** (Δ9-THC) reduced opioid receptor binding, evaluated in intact cells, by ≈ 40 -45% in cells exposed for 24 h to 50 and 100 nM Δ9-THC and by ≈ 25% in cells exposed to 10 nM Δ9-THC. Lower doses of Δ9-THC (0.1 and 1 nM) or a shorter exposure time to the cannabinoid (6 h) were not effective. Down-regulation of δ opioid receptors was not observed in cells exposed for 24 h to pertussis toxin (PTX) and then **treated** for 24 h with 100 nM Δ9-THC. In cells that were exposed for 24 h to the cannabinoid, the ability of Δ9-THC and of the δ opioid receptor agonist [D-Ser2, Leu5, Thr6]enkephalin to inhibit forskolin-stimulated cAMP accumulation was significantly attenuated. Prolonged exposure of NG 108-15 cells to 100 nM Δ9-THC produced a significant elevation of steady-state levels of δ opioid receptor mRNA. This effect was not observed in cells **pretreated** with PTX. The selective cannabinoid receptor antagonist SR 141716A blocked the effects elicited by Δ9-THC on δ opioid receptor desensitization, down-regulation and gene expression; thus indicating that

these are mediated via activation of cannabinoid receptors. These data demonstrate the existence, in NG 108-15 cells, of a complex cross-talk between the cannabinoid and opioid receptors on prolonged exposure to Δ9-THC triggered by changes in signaling through Gi and/or G0-coupled receptors.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:239514 HCAPLUS
DOCUMENT NUMBER: 126:312129
TITLE: Receptor mediation in cannabinoid stimulated arachidonic acid mobilization and anandamide synthesis
AUTHOR(S): Hunter, Sheila A.; Burstein, Sumner H.
CORPORATE SOURCE: Dep. Biochem., Univ. Massachusetts Med. Sch., Worcester, MA, 01655-0103, USA
SOURCE: Life Sciences (**1997**), 60(18), 1563-1573
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous reports have suggested that increased synthesis of eicosanoids is a significant effect of cannabinoids in several models including the human. To address the question of receptor mediation in this process we have carried out expts. using oligonucleotides that are antisense to the CB1 and to the CB2 receptors. We have synthesized sense, antisense and random oligonucleotide probes to test for receptor involvement in THC stimulation of arachidonic acid release in three cell lines of both central and peripheral origin. **Treatment** of N18 mouse **neuroblastoma** cells with the CB1 antisense probe, at two concns., resulted in a dramatic decrease of THC stimulated arachidonate release while **treatment** with antisense CB2 was less effective. Synthesis of the novel eicosanoid, anandamide, was also reduced by antisense CB1 but not by antisense CB2. Western blot anal. indicated a decreased level of CB1 in CB1 antisense **treated** cells. The CB1 antagonist, SR141716A, was effective in reducing the THC elevated levels of free arachidonate in these cells in agreement with the antisense data. In the macrophage line, RAW 264.7, we found that while the sense, the random and the CB1 antisense oligonucleotides were ineffective, the CB2 antisense probe gave significant redns. of the THC induced response. The CB2 probe was also effective in reducing the release of arachidonate in WI-38 human lung fibroblasts. These findings support the idea of a receptor mediated process for cannabinoid stimulation of eicosanoid synthesis.

L26 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:711866 HCAPLUS
DOCUMENT NUMBER: 126:1046
TITLE: Tau protein for delta-9 **tetrahydrocannabinol** in a human **neuroblastoma** cell line
AUTHOR(S): Lew, G. M.
CORPORATE SOURCE: College Human Medicine, Michigan State Univ., East Lansing, MI, 48824, USA
SOURCE: General Pharmacology (**1996**), 27(7), 1141-1143
CODEN: GEPHDP; ISSN: 0306-3623
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1. A human **neuroblastoma** cell line, SH-SY5Y, was used to determine the effects of delta-9-**tetrahydrocannabinol** (THC) on microtubule-associated tau protein. 2. After 48-h **treatment**, THC (10-9 M) decreased 50 kD tau protein in the cytoplasmic (supernatant) fraction, and in the membrane (pellet) fraction the drug (10-7 M) also decreased 50 kD tau protein. 3. This reduction in tau protein was accompanied by a 27% reduction ($P<0.05$) in the membrane (pellet) total protein after (10-7 M) THC and a 28% increase ($P<0.02$) in cytoplasmic (supernatant) total protein after 10-9 M THC.

L26 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:578313 HCAPLUS
DOCUMENT NUMBER: 125:266063
TITLE: Hormonal **treatment** in advanced non-small cell lung cancer: Fact or fiction?
AUTHOR(S): Vansteenkiste, J. F.; Simons, J. P.; Wouters, E. F.; Demedts, M. G.
CORPORATE SOURCE: University Hospital Gasthuisberg, Catholic University, Louvain, B-3000, Belg.
SOURCE: European Respiratory Journal (**1996**), 9(8), 1707-1712
CODEN: ERJOEI; ISSN: 0903-1936
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 48 refs. In patients with advanced non-small cell lung cancer, cachexia is an important cause of morbidity and mortality. The pathogenic mechanism of this finding, usually referred to as "cancer anorexia and cachexia syndrome" (CACS), is complex and far from completely understood, but a disturbed equilibrium between possible food intake and metabolic needs seems to be fundamental. The literature data on the **treatment** options in advanced non-small cell lung cancer (NSCLC) with cachexia are reviewed. Based on the clin. studies on cancer cachexia, some recommendations for the **therapeutic** approach of this disorder in patients with advanced NSCLC can be given. Metoclopramide is easily administered, can alleviate gastric disturbances, but probably does not correct the catabolic spiral of CACS. There are not enough data to advise the use of parenteral nutritional support, hydrazine, cyproheptadine, **tetrahydrocannabinol** or nandrolone decanoate. Corticosteroids are useful in addnl. analgesia and fast palliation of very weak and debilitated patients in the final episode of their disease. Recent data in non-small cell lung cancer patients are in favor of the use of high-dose progestagens to **improve** both appetite and weight

L26 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:983441 HCAPLUS
DOCUMENT NUMBER: 124:76301
TITLE: Activation of mitogen-activated protein kinases by stimulation of the central cannabinoid receptor CB1
AUTHOR(S): Bouaboula, Monsif; Poinot-Chazel, Caroline; Bourrie, Bernard; Canat, Xavier; Calandra, Bernard; Rinaldi-Carmona, Murielle; Le Fur, Gerard; Casellas, Pierre
CORPORATE SOURCE: Sanofi Recherche, Dep. Immunopharmacology, Montpellier, 34184, Fr.
SOURCE: Biochemical Journal (**1995**), 312(2), 637-41
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The G-protein-coupled central cannabinoid receptor (CB1) has been shown to be functionally associated with several biol. responses including inhibition of adenylate cyclase, modulation of ion channels and induction of the immediate-early gene Krox-24. Using stably transfected Chinese Hamster Ovary cells expressing human CB1 we show here that cannabinoid **treatment** induces both phosphorylation and activation of mitogen-activated protein (MAP) kinases, and that these effects are inhibited by SR 141716A, a selective CB1 antagonist. The two p42 and p44 kDa MAP kinases are activated in a time- and dose-dependent manner. The rank order of potency for the activation of MAP kinases with various cannabinoid agonists is CP-55940 > Δ9- **tetrahydrocannabinol** > WIN 55212.2, in agreement with the pharmacol. profile of CB1. The activation of MAP kinases is blocked by pertussis toxin but not by **treatment** with hydrolysis-resistant cAMP analogs. This suggests that the signal transduction pathway between CB1 and MAP kinases involves a pertussis-toxin-sensitive GTP-binding protein and is independent of cAMP metabolism This coupling of CB1 subtype and mitogenic signal pathway, also observed in the human **astrocytoma** cell line U373 MG, may explain the mechanism of action underlying cannabinoid-induced Krox-24 induction.

L26 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:367242 HCAPLUS
DOCUMENT NUMBER: 122:151262
TITLE: Low doses of anandamides inhibit pharmacological effects of Δ9- **tetrahydrocannabinol**
AUTHOR(S): Fride, E.; Barg, J.; Levy, R.; Saya, D.; Heldman, E.; Mechoulam, R.; Vogel, Z.
CORPORATE SOURCE: Medical Faculty, Hebrew University Jerusalem, Jerusalem, 91120, Israel
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1995**), 272(2), 699-707
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been shown previously that the endogenous cannabinoid receptor ligand arachidonylethanolamide (anandamide 20:4, n-6) induces in vivo and in vitro effects typical of a cannabinoid partial agonist. We now report that the synthetic docosahexaenylethanolamide (anandamide 22:6, n-3) shows similar activities. In addition we show that these two anandamides, under certain exptl. conditions, antagonize the effects of Δ9-THC both in vivo and in vitro. Thus a significant decrease in the potency of Δ9-THC-induced inhibition of adenylate cyclase was observed in N18TG2 **neuroblastoma** cells that were **pretreated** with low concns. of anandamides. At these low concns. of anandamides had no effect when applied alone. In vivo, Sabra or ICR mice were subjected to a tetrad of tests, designed to detect cannabinoid-induced effects. Mice **pretreated** (i.p.) with 10 mg/kg of Δ9-THC received injections with anandamides. Only low doses (0.0001-0.1 mg/kg) of the anandamides, which had no effects when administered alone, partially or fully inhibited the THC-induced effects. These findings suggest that the inhibition of Δ9-THC-induced effects by low doses of anandamides may be due to their partial agonistic effects. It is possible that low doses of the anandamides are capable of activating a Gs protein mediated signaling pathway, or may cause an allosteric modulation of the cannabinoid receptor.

L26 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:473911 HCAPLUS
DOCUMENT NUMBER: 121:73911
TITLE: Inhibitors of arachidonic acid metabolites for preventing neurological damage, and screening method for neuroprotectants
INVENTOR(S): Bernton, Edward W.; Jett, Marti; Gendelman, Howard
PATENT ASSIGNEE(S): United States Department of the Army, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9412667	A1	19940609	WO 1993-US11542	19931129 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1992-982656 A	19921127 <--
			US 1993-61970 A	19930902 <--

AB A method is provided for **treating** encephalitis or encephalopathy secondary to CNS infection by administration of **therapeutically** effective amts. of compns. which inhibit the release of platelet activation factor and/or arachidonate metabolites. Compns. are disclosed containing e.g. 11-nor-**.DELTA.8-tetrahydrocannabinol**-9-carboxylic acid or nordihydroguaiaretic acid. Also provided are methods for screening for compds. that have neuroprotective activity; the methods comprise infecting monocytes or lymphocytes with an infectious organism known to cause neural damage, adding the resulting infected culture to a culture of astrocyte cells, adding a test compound, allowing sufficient time to pass for the production of TNF-alpha, withdrawing aliquots from the supernatant of the culture, adding the aliquots to cultures of neural cells and identifying which supernatants impart a neuroprotective effect.

L26 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:420323 HCAPLUS
DOCUMENT NUMBER: 117:20323
TITLE: Cannabinoids inhibit N-type calcium channels in **neuroblastoma**-glioma cells
AUTHOR(S): Mackie, Ken; Hille, Bertil
CORPORATE SOURCE: Sch. Med., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1992**), 89(9), 3825-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The psychoactive properties of Cannabis sativa and its major biol. active constituent, Δ9- **tetrahydrocannabinol**, have been known for years. The recent identification and cloning of a specific cannabinoid receptor suggest that cannabinoids mimic endogenous compds. affecting neural signals for mood, memory, movement, and pain. Using whole-cell voltage clamp and the cannabinomimetic aminoalkylindole WIN 55,212-2, it has been found that cannabinoid receptor activation reduces the amplitude of voltage-gated calcium currents in the **neuroblastoma**-glioma cell line NG108-15. The inhibition is potent, being half-maximal at less

than 10 nM, and reversible. The inactive enantiomer, WIN 55,212-3, does not reduce calcium currents even at 1 μM. Of the several types of calcium currents in NG108-15 cells, cannabinoids predominantly inhibit an ω-conotoxin-sensitive, high-voltage-activated calcium current. Inhibition was blocked by incubation with pertussis toxin but was not altered by prior **treatment** with hydrolysis-resistant cAMP analogs together with a phosphodiesterase inhibitor, suggesting that the transduction pathway between the cannabinoid receptor and calcium channel involves a pertussis toxin-sensitive GTP-binding protein and is independent of cAMP metabolism However, the development of inhibition is considerably slower than a pharmacol. similar pathway used by an α2-adrenergic receptor in these cells. Results suggest that inhibition of N-type calcium channels, which could decrease excitability and neurotransmitter release, may underlie some of the psychoactive effects of cannabinoids.

L26 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:526814 HCAPLUS
DOCUMENT NUMBER: 115:126814
TITLE: Marijuana decreases macrophage antiviral and antitumor activities
AUTHOR(S): Cabral, G. A.; Vasquez, R.
CORPORATE SOURCE: Med. Coll. Virginia, VCU, Richmond, VA, 23298-0678, USA
SOURCE: Advances in the Biosciences (Oxford) (**1991**), 80(Physiopathol. Illicit Drugs: Cannabis, Cocaine, Opiates), 93-105
CODEN: AVBIB9; ISSN: 0065-3446
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Delta-9-**tetrahydrocannabinol** (THC), the major psychoactive component of marijuana, was shown to decrease macrophage functional competence against tumor cells and virus-infected cells. Peritoneal macrophages of :(B6C3)F1 mice receiving Propionibacterium acnes as a macrophage "activator" and **treated** with THC (50 mg/kg and 100 mg/kg) exhibited a dose-related decrease in effector cell:target cell contact-dependent tumoricidal activity against rat B103 **neuroblastoma** cells. Macrophage-like cells of the lines J774A.1, P388D1, or RAW264.7 exposed in vitro to THC exhibited decreased extrinsic antiviral activity to herpes simplex virus type 2. SEM demonstrated that THC administered in vivo or in vitro did not prevent P. acnes macrophages or the macrophage-like cells from attaching to tumor or virus-infected target cells. However, the drug inhibited protein expression by macrophages in response to stimuli such as P. acnes in vivo and bacterial lipopolysaccharide in vitro. These results suggest that THC inhibits "full" activation of macrophages since tumoricidal and antiviral activities are characteristic features of macrophage "full" activation. Furthermore, since contact-dependent tumoricidal and extrinsic antiviral activities are two-step processes in which effector cell:target cell conjugation is followed by delivery of effector mols., these results indicate that the cannabinoid acted at the level of inhibition of effector mol. expression.

L26 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:48399 HCAPLUS
DOCUMENT NUMBER: 112:48399
TITLE: The effect of marijuana smoke exposure on murine **sarcoma** 180 survival in Fisher rats
AUTHOR(S): Watson, E. Sue

CORPORATE SOURCE: Res. Inst. Pharm. Sci., Sch. Pharm., University, MS, 38677, USA
SOURCE: Immunopharmacology and Immunotoxicology (**1989**), 11(2-3), 211-22
CODEN: IITOEF; ISSN: 0892-3973
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fisher rats were **treated** for 28 or 60 days to multiple exposures to the smoke of marijuana or marijuana placebo cigarettes. Primary, secondary and in some instances tertiary tumor implants were performed. Murine **sarcoma** 180 tumor cells (7.5 + 107) were implicated s.c. on day 1, 14 and 28 following initiation of smoke exposure (28 day studies) or on day 1, 14 after cessation of smoke exposure (60 day studies). Tumor areas were measured on alternate days beginning on the second or third day after implantation for 13 or 14 days. Exposure to both marijuana and placebo smoke for 28 days (6, 9 and 18 cigarettes per day) resulted in suppressed growth of secondary and tertiary implants. Administration of Δ9- **tetrahydrocannabinol** (50 mg/kg, i.p., 20 days) failed to suppress the growth of primary and secondary tumors. This suggests that noncannabinoid constituents of the smoke may contribute to the suppression of tumor growth. Exposure of rats to 9, but not 4 or 6, marijuana or placebo cigarettes per day for 60 days suppressed the growth of primary but not secondary tumors. Thus, the effects of smoke exposure appear to be lose by 2 wk after cessation of **treatment.** The possible existence of a non-cannabinoid immunostimulant in the smoke is discussed.

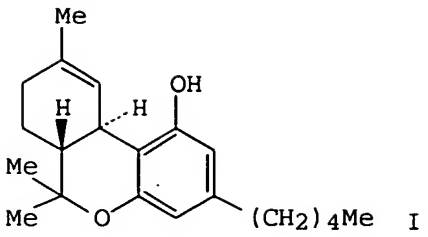
L26 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:198239 HCAPLUS
DOCUMENT NUMBER: 108:198239
TITLE: Regulation of adenylate cyclase by chronic exposure to cannabimimetic drugs
AUTHOR(S): Dill, Jill A.; Howlett, Allyn C.
CORPORATE SOURCE: Sch. Med., St. Louis Univ., St. Louis, MO, 63104, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1988**), 244(3), 1157-63
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Short-term exposure to either Δ9-THC or the more potent nantradol analog, desacetyllevonantradol (DALN), at ≤100 μM did not compromise the plating efficiency of **neuroblastoma** cells. Cells that were exposed to 1 μM Δ9-THC (maximally effective for inhibiting cAMP production) for 24 h in a serum-free medium were shown to accumulate the drug but not to metabolize it. Exposure to 10 μM Δ9-THC or DALN for up to 48 h failed to affect cell growth rate or protein content per cell. The gross morphol. of cannabinoid-**treated** cells was not altered at the light or the electron microscope level. The cellular organelles and membranes appeared intact, with no remarkable differences from control cells. The inhibition of cAMP accumulation in response to cannabimimetic drugs was diminished in cells **treated** with Δ9-THC or DALN for 24 h. This desensitization was homologous because both Δ9-THC and DALN responses were attenuated after exposure to either cannabimimetic drug. In contrast, the inhibition of cAMP accumulation in response to carbachol via the muscarinic receptor was unaltered by previous exposure of the cells to cannabimimetic agents. For DALN, the desensitization could be observed as early as 4 h and was dose-dependent. These studies demonstrate that desensitization of the cannabimimetic regulation of adenylate cyclase can

occur in the absence of cytotoxicity.

L26 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:629021 HCAPLUS
DOCUMENT NUMBER: 107:229021
TITLE: Interaction of delta-9-**tetrahydrocannabinol** with rat B103 **neuroblastoma** cells
AUTHOR(S): Cabral, Guy A.; McNerney, Peter J.; Mishkin, Eric M.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
SOURCE: Archives of Toxicology (**1987**), 60(6), 438-49
CODEN: ARTODN; ISSN: 0340-5761
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of Δ9- **tetrahydrocannabinol** (Δ9-THC) on the growth kinetics and morphol. of rat B103 **neuroblastoma** cells was assessed. Δ9-THC in doses ranging from 10-4 to 10-7 M inhibited cellular growth in a dose-dependent fashion as evidenced by delay in doubling time, decrease in saturation d., and decrease in efficiency of plating. The inhibition in cellular growth was paralleled by dose-related alterations in cell morphol. Modifications included rounding of cells, retraction of neurites, blebbing of the cell surface, and exfoliation of the plasma membrane. Cytoplasmic alterations included distension of the endoplasmic reticulum, Golgi apparatus, and perinuclear space, and macrovacuolization. Intracytoplasmic laminated inclusions and vesicular clusters were suggestive of membrane repair in drug-**treated** cells. These morphol. changes were accompanied by cytoskeletal rearrangement in the absence of significant alteration in the concentration of total cytoskeletal protein. Autoradiog. examination of the intracellular fate of 3H-Δ9-THC demonstrated that the drug was confined to the cytoplasmic compartment and often associated with macrovacuoles. These results suggest that Δ9-THC interacts with cellular membranes, thereby altering **neuroblastoma** cell growth and behavior. The results are discussed in relation to drug interactions and herpes simplex virus 2 infection.

L26 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:448191 HCAPLUS
DOCUMENT NUMBER: 101:48191
TITLE: Influence of Δ9- **tetrahydrocannabinol** on expression of histone and ribosomal genes in normal and transformed human cells
AUTHOR(S): Green, Linda G.; Stein, Janet L.; Stein, Gary S.
CORPORATE SOURCE: Coll. Med., Univ. Florida, Gainesville, FL, 32610, USA
SOURCE: Biochemical Pharmacology (**1984**), 33(7), 1033-40
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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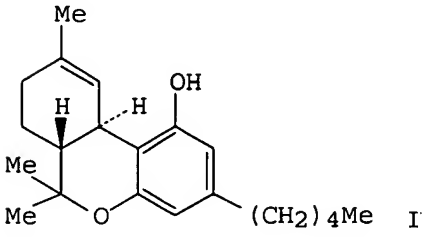
AB The influence of Δ9-THC (I) [1972-08-3] on the cellular levels of histone mRNAs and rRNAs was examined in several normal and transformed human cell lines-HeLa S3 cells, WI-38 human diploid fibroblasts, SV40-transformed WI-38 cells, and A549 lung **carcinoma** cells. **Treatment** with Δ9-THC (10-40 μM) for 10 h resulted in a concentration-dependent decrease in the representation of H2A, H2B, H3 and H4 histone mRNAs without a significant inhibitory effect on the levels of rRNAs. The cannabinoid-mediated inhibitory effect on histone gene expression was less evident in cells with active drug-metabolizing systems.

L26 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:69581 HCAPLUS
DOCUMENT NUMBER: 92:69581
TITLE: Long term effects of Δ9-**tetrahydrocannabinol** in mice
AUTHOR(S): Szepsenwol, J.; Fletcher, J.; Murison, G. L.; Toro-Goyco, E.
CORPORATE SOURCE: Dep. Biol. Sci., Florida Int. Univ., Miami, FL, USA
SOURCE: Advances in the Biosciences (Oxford) (**1979**), Volume Date 1978, 22-23(Marihuana: Biol. Eff.), 359-70
CODEN: AVBIB9; ISSN: 0065-3446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

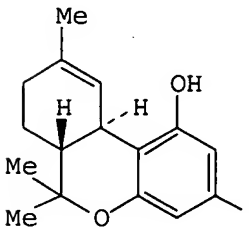


I

AB Δ9- **Tetrahydrocannabinol** (I) [1972-08-3] (20 μg/0.05 mL sesame oil/wk, s.c.) unlike estrogen did not interfere with the normal development or reproduction of C57 B1/6 and BALB/c mice. It caused, however, a high mortality rate among the offspring. This was particularly high among the C57 B1/6 strain and was apparently due to an inhibitory effect upon the milk secretion by the mammary gland, since newborn C57 B1/6 mice which had no milk in their stomachs the day after birth survived and developed normally when foster nursed by lactating BALB/c females. Four

of 200 BALB/c I-**treated** mice developed **fibrosarcomas** at the point of injection of the drug. Of 46 C57 B1/6 I-**treated** mice, 1 developed a mammary **adenocarcinoma**.. Of the 32 BALB/c females receiving injections of sesame oil, 8 developed mammary **adenocarcinomas**. Thus, it is thought that sesame oil had an estrogenic effect; it causes mammary carcinogenesis by increasing the production of LH and LTH. I appears to have an antiestrogenic effect, causing a decrease in LH and LTH, which is the cause of defective secretion of milk by the mammary glands and the high mortality of the offspring, particularly of the C57 B1/6 mice. In addition, I appears to have a carcinogenic effect by stimulating development of mesenchymal tumors. Its effect upon parenchymal tumors may be inhibitory.

L26 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:164045 HCAPLUS
DOCUMENT NUMBER: 88:164045
TITLE: In vivo effects of cannabinoids on macromolecular biosynthesis in Lewis lung **carcinomas**
AUTHOR(S): Friedman, Marvin A.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, USA
SOURCE: Cancer Biochemistry Biophysics (**1977**), 2(2), 51-4
CODEN: CABCD4; ISSN: 0305-7232
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

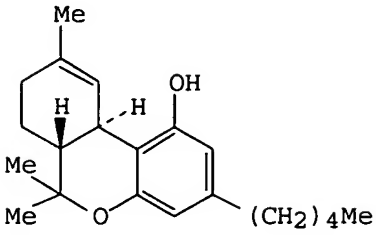


I

AB The effects of Δ9-THC (I) [1972-08-3]Δ8-THC [**5957-75-5**], and **cannabidiol** [**13956-29-1**] on tumor macromol. biosynthesis in mice bearing Lewis lung **carcinomas** were studied. The drugs inhibited thymidine-3H incorporation into DNA acutely, but did not inhibit leucine uptake into tumor protein. At 24 h after **treatment**, cannabinoids did not inhibit thymidine-3H incorporation into DNA, leucine-3H uptake into protein or cytidine-3H into RNA.

L26 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:487170 HCAPLUS
DOCUMENT NUMBER: 85:87170
TITLE: Effects of Δ9- **tetrahydrocannabinol** in Lewis lung **adenocarcinoma** cells in tissue culture
AUTHOR(S): White, A. C.; Munson, J. A.; Munson, A. E.; Carchman, R. A.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, USA

SOURCE: Journal of the National Cancer Institute (1940-1978) (**1976**), 56(3), 655-8
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB There was a dose-related decrease in DNA synthesis in transformed cell cultures **treated** with Δ9- **tetrahydrocannabinol** (I) [1972-08-3]. The decrease, observed over a 4-hour period, was not accompanied by a change in the radioactive precursor pool as compared to that of control cultures. The distribution of labeled products clearly differed from that observed after **treatment** with cytosine arabinoside [147-94-4]. I inhibited DNA synthesis at some point beyond the uptake of 3H-thymidine.

```
=> d que stat l31
L20             1 SEA FILE=REGISTRY ABB=ON  Δ8-TETRAHYDROCANNABINOL/CN
L21             2 SEA FILE=REGISTRY ABB=ON  (CANNABINOL OR CANNABIDIOL)/CN
L22             3 SEA FILE=REGISTRY ABB=ON  L20 OR L21
L23          5906 SEA FILE=HCAPLUS ABB=ON  L22 OR (Δ8-TETRAHYDROCANNABINOL?
                  OR ?CANNABINOL? OR ?CANNABIDIOL?)
L24            68 SEA FILE=HCAPLUS ABB=ON  L23 AND (?BLASTOMA? OR ?EPITHELOMA?
                  OR ?GERMINOMA? OR ?CARCINOMA? OR ?ASTROCYTOMA? OR ?EPENDYMOMA?
                  OR ?OLIGODENROGLIOMA? OR ?OLIGODENDROGLIOMA? OR ?NEUROEPITHELOM
                  A? OR ?NEUROECTODERM?(W)(?TUMOR? OR ?TUMOUR?) OR ?MENINGIOMA?
                  OR ?SARCOMA? OR ?MELANOMA? OR ?SCHWANOMA?)
L25            29 SEA FILE=HCAPLUS ABB=ON  L24 AND (?THERAP? OR ?TREAT? OR
                  ?CURE? OR ?IMPROV?)
L27           150 SEA L25
L28            74 DUP REMOV L27 (76 DUPLICATES REMOVED)
L29            29 SEA L28 AND (?GLIOBLASTOMA? OR ?MEDUL?(W) ?EPITHELOMA? OR
                  ?MEDULOBLASTOMA? OR ?NEUROBLASTOMA? OR ?GERMINOMA? OR ?EMBROYOC
                  ARCINOMA? OR ?ASTROCYTOMA? OR ?ASTROBLASTOMA? OR ?EPENDYMOMA?
                  OR ?OLIGODENROGLIOMA? OR ?PLEXOCARCINOMA? OR ?NEUROEPITHELOMA?
                  OR ?PINEOBLASTOMA? OR ?EPANDIMOBLASTOMA?)
L30             1 SEA L28 AND (?NEUROECTODERM?(W)(?TUMOR? OR ?TUMOUR?) OR
                  ?MALIGN?(W)(?MENINGIOMA? OR ?MELANOMA? OR ?SCHWANOMA?) OR
                  ?CHONDROSARCOMA? OR ?MENINGEAL?(W) ?SARCOM?)
L31            30 SEA L29 OR L30

=> d ibib abs l31 1-30

L31  ANSWER 1 OF 30     MEDLINE on STN
ACCESSION NUMBER:   2004408103     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15313899
TITLE:              Cannabinoids inhibit the vascular endothelial growth factor
                    pathway in gliomas.
AUTHOR:             Blazquez Cristina; Gonzalez-Feria Luis; Alvarez Luis; Haro
                    Amador; Casanova M Llanos; Guzman Manuel
CORPORATE SOURCE:   Department of Biochemistry and Molecular Biology I, School
                    of Biology, Complutense University, Madrid, Spain.
SOURCE:             Cancer research, (2004 Aug 15) 64 (16) 5617-23.
                    Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200409
ENTRY DATE:         Entered STN: 20040818
                    Last Updated on STN: 20041001
                    Entered Medline: 20040930
AB   Cannabinoids inhibit tumor angiogenesis in mice, but the mechanism of
     their antiangiogenic action is still unknown. Because the vascular
     endothelial growth factor (VEGF) pathway plays a critical role in tumor
     angiogenesis, here we studied whether cannabinoids affect it. As a first
     approach, cDNA array analysis showed that cannabinoid administration to
     mice bearing s.c. gliomas lowered the expression of various VEGF
     pathway-related genes. The use of other methods (ELISA, Western blotting,
     and confocal microscopy) provided additional evidence that cannabinoids
     depressed the VEGF pathway by decreasing the production of VEGF and the
     activation of VEGF receptor (VEGFR)-2, the most prominent VEGF receptor,
     in cultured glioma cells and in mouse gliomas. Cannabinoid-induced
     inhibition of VEGF production and VEGFR-2 activation was abrogated both in
     vitro and in vivo by pharmacological blockade of ceramide biosynthesis.
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These changes in the VEGF pathway were paralleled by changes in tumor size. Moreover, intratumoral administration of the cannabinoid Delta9-**tetrahydrocannabinol** to two patients with **glioblastoma** multiforme (grade IV **astrocytoma**) decreased VEGF levels and VEGFR-2 activation in the tumors. Because blockade of the VEGF pathway constitutes one of the most promising antitumoral approaches currently available, the present findings provide a novel pharmacological target for cannabinoid-based **therapies.**

L31 ANSWER 2 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2004133485 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15026328
TITLE: Cannabinoids induce cancer cell proliferation via tumor necrosis factor alpha-converting enzyme (TACE/ADAM17)-mediated transactivation of the epidermal growth factor receptor.
AUTHOR: Hart Stefan; Fischer Oliver M; Ullrich Axel
CORPORATE SOURCE: Department of Molecular Biology, Max-Planck-Institute of Biochemistry, Am Klopferspitz 18A, D-82152 Martinsried, Germany.
SOURCE: Cancer research, (2004 Mar 15) 64 (6) 1943-50. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040318
Last Updated on STN: 20040409
Entered Medline: 20040408

AB Cannabinoids, the active components of marijuana and their endogenous counterparts were reported as useful analgetic agents to accompany primary cancer **treatment** by preventing nausea, vomiting, and pain and by stimulating appetite. Moreover, they have been shown to inhibit cell growth and to induce apoptosis in tumor cells. Here, we demonstrate that anandamide, Delta(9)-**tetrahydrocannabinol** (THC), HU-210, and Win55,212-2 promote mitogenic kinase signaling in cancer cells. **Treatment** of the **glioblastoma** cell line U373-MG and the lung **carcinoma** cell line NCI-H292 with nanomolar concentrations of THC led to accelerated cell proliferation that was completely dependent on metalloprotease and epidermal growth factor receptor (EGFR) activity. EGFR signal transactivation was identified as the mechanistic link between cannabinoid receptors and the activation of the mitogen-activated protein kinases extracellular signal-regulated kinase 1/2 as well as prosurvival protein kinase B (Akt/PKB) signaling. Depending on the cellular context, signal cross-communication was mediated by shedding of proAmphiregulin (proAR) and/or proHeparin-binding epidermal growth factor-like growth factor (proHB-EGF) by tumor necrosis factor alpha converting enzyme (TACE/ADAM17). Taken together, our data show that concentrations of THC comparable with those detected in the serum of patients after THC administration accelerate proliferation of cancer cells instead of apoptosis and thereby contribute to cancer progression in patients.

L31 ANSWER 3 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2003285375 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12813001
TITLE: Reduction of human monocytic cell neurotoxicity and cytokine secretion by ligands of the cannabinoid-type CB2 receptor.

AUTHOR: Klegeris Andis; Bissonnette Christopher J; McGeer Patrick L
CORPORATE SOURCE: Kinsmen Laboratory of Neurological Research, University of British Columbia, 2255 Westbrook Mall, Vancouver, BC, Canada V6T 1Z3.
SOURCE: British journal of pharmacology, (2003 Jun) 139 (4) 775-86. Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20030619
Last Updated on STN: 20040325
Entered Medline: 20040324

AB 1 Two cannabinoid receptors, CB1 and CB2, have been identified. The CB1 receptor is preferentially expressed in brain, and the CB2 receptor in cells of leukocyte lineage. We identified the mRNA for the CB1 receptor in human **neuroblastoma** SH-SY5Y cells, and the mRNA and protein for the CB2 receptor in human microglia and THP-1 cells. 2 Delta(9)-and **Delta(8)-tetrahydrocannabinol** (THC) were toxic when added directly to SH-SY5Y **neuroblastoma** cells. The toxicity of Delta(9)- THC was inhibited by the CB1 receptor antagonist SR141716A but not by the CB2 receptor antagonist SR144528. The endogenous ligand anandamide was also toxic, and this toxicity was enhanced by inhibitors of its enzymatic hydrolysis. 3 The selective CB2 receptor ligands JWH-015 and indomethacin morpholinylamide (BML-190), when added to THP-1 cells before stimulation with lipopolysaccharide (LPS) and IFN-gamma, reduced the toxicity of their culture supernatants to SH-SY5Y cells. JWH-015 was more effective against neurotoxicity of human microglia than THP-1 cells. The antineurotoxic activity of JWH-015 was blocked by the selective CB2 receptor antagonist SR144528, but not by the CB1 receptor antagonist SR141716A. This activity of JWH-015 was synergistic with that of the 5-lipoxygenase (5-LOX) inhibitor REV 5901. 4 Cannabinoids inhibited secretion of IL-1beta and tumor necrosis factor-alpha (TNF-alpha) by stimulated THP-1 cells, but these effects could not be directly correlated with their antineurotoxic activity. 5 Specific CB2 receptor ligands could be useful anti-inflammatory agents, while avoiding the neurotoxic and psychoactive effects of CB1 receptor ligands such as Delta(9)-THC.

L31 ANSWER 4 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2002409124 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12163181
TITLE: CB1 cannabinoid receptor-mediated tyrosine phosphorylation of focal adhesion kinase-related non-kinase.
AUTHOR: Zhou Dan; Song Z H
CORPORATE SOURCE: Department of Pharmacology and Toxicology, School of Medicine, University of Louisville, Louisville, KY 40292, USA.
CONTRACT NUMBER: DA-11511 (NIDA)
SOURCE: FEBS letters, (2002 Aug 14) 525 (1-3) 164-8. Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020807
Last Updated on STN: 20020921

Entered Medline: 20020920

AB The effect of cannabinoid on the tyrosine phosphorylation of focal adhesion kinase (FAK) and focal adhesion kinase-related non-kinase (FRNK) was investigated in differentiated mouse **neuroblastoma** N1E-115 cells. HU-210, a potent cannabinoid agonist, elicited a time-dependent enhancement of tyrosine phosphorylation of FRNK, but not FAK. **Pretreatment** of cells with antisense oligodeoxynucleotide targeting CB1 cannabinoid receptor abolished HU-210-induced FRNK tyrosine phosphorylation. In addition, **pretreatment** of cells with 8-Br-cAMP also blocked HU-210-induced FRNK tyrosine phosphorylation. These data demonstrated that HU-210 induces FRNK tyrosine phosphorylation by activating G(i)-coupled CB1 cannabinoid receptor in N1E-115 cells. This newly discovered, cannabinoid-induced FRNK tyrosine phosphorylation might be a novel mechanism for cannabinoid-induced functional changes.

L31 ANSWER 5 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2001446068 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11494371
TITLE: CB1 cannabinoid receptor-mediated neurite remodeling in mouse **neuroblastoma** N1E-115 cells.
AUTHOR: Zhou D; Song Z H
CORPORATE SOURCE: Department of Pharmacology and Toxicology, School of Medicine, University of Louisville, KY 40292, USA.
CONTRACT NUMBER: DA-11511 (NIDA)
SOURCE: Journal of neuroscience research, (2001 Aug 15) 65 (4) 346-53.
Journal code: 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010917
Entered Medline: 20010913

AB The morphological remodeling of neuronal cells influences neurogenesis and brain functions. We hypothesize that psychoactive and neurotoxic effects of cannabinoids may be mediated, at least in part, by their morphoregulatory activities. In the present study, mouse **neuroblastoma** N1E-115 cells were used as an in vitro model to investigate cannabinoid-induced neurite remodeling effects and to identify the involvement of cannabinoid receptors in this neurite remodeling process. Using reverse transcription-polymerase chain reaction and immunofluorescence microscopy, the endogenously expressed CB1, but not CB2, cannabinoid receptors were detected in morphologically differentiated N1E-115 cells. Activation of these natively expressed CB1 cannabinoid receptors by cannabinoid agonist HU-210 led to a concentration-dependent inhibition of adenylate cyclase activity. Importantly, HU-210 **treatment** induced neurite retraction in a concentration-dependent manner. **Pretreatment** of N1E-115 cells with a CB1 antisense oligodeoxynucleotide (ODN) suppressed HU-210-induced inhibition of forskolin-stimulated cAMP accumulation, indicating that the knocking down of functional CB1 cannabinoid receptor expression was achieved. Antisense ODN **pretreatment** also abolished HU-210-induced neurite retraction, demonstrating the involvement of CB1 cannabinoid receptors in mediating the neurite remodeling effects of HU-210. In addition, reversing HU-210-induced intracellular cAMP declination by 8-Br-cAMP partially prevented HU-210-induced neurite retraction, indicating the involvement of cAMP-dependent signaling pathways in mediating the neurite

remodeling function of CB1 cannabinoid receptors in N1E-115 cells. These data demonstrate that neurite remodeling is a newly discovered function of CB1 cannabinoid receptors. This morphoregulatory function of CB1 cannabinoid receptors might be a new mechanism that mediates the psychoactive and neurotoxic effects of cannabinoids in developing and adult brain.

L31 ANSWER 6 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2001299575 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11309246
TITLE: Characterization of palmitoylethanolamide transport in mouse Neuro-2a **neuroblastoma** and rat RBL-2H3 basophilic leukaemia cells: comparison with anandamide.
AUTHOR: Jacobsson S O; Fowler C J
CORPORATE SOURCE: Department of Pharmacology and Clinical Neuroscience, Umea University, SE-901 87 Umea, Sweden..
stig.jacobsson@pharm.umu.se
SOURCE: British journal of pharmacology, (2001 Apr) 132 (8) 1743-54.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB The endogenous cannabinoid receptor agonist anandamide (AEA) and the related compound palmitoylethanolamide (PEA) are inactivated by transport into cells followed by metabolism by fatty acid amide hydrolase (FAAH). The cellular uptake of AEA has been characterized in detail, whereas less is known about the properties of the PEA uptake, in particular in neuronal cells. In the present study, the pharmacological and functional properties of PEA and AEA uptake have been investigated in mouse Neuro-2a **neuroblastoma** and, for comparison, in rat RBL-2H3 basophilic leukaemia cells. Saturable uptake of PEA and AEA into both cell lines were demonstrated with apparent K(M) values of 28 microM (PEA) and 10 microM (AEA) in Neuro-2a cells, and 30 microM (PEA) and 9.3 microM (AEA) in RBL-2H3 cells. Both PEA and AEA uptake showed temperature-dependence but only the AEA uptake was sensitive to **treatment** with Pronase and phenylmethylsulfonyl fluoride. The AEA uptake was inhibited by AM404, 2-arachidonoylglycerol (2-AG), R1- and S1-methanandamide, arachidonic acid and olvanil with similar potencies for the two cell types. PEA, up to a concentration of 100 microM, did not affect AEA uptake in either cell line. AEA, 2-AG, arachidonic acid, R1-methanandamide, (9)-THC, and **cannabidiol** inhibited PEA transport in both cell lines. The non-steroidal anti-inflammatory drug indomethacin inhibited the AEA uptake but had very weak effects on the uptake of PEA. From these data, it can be concluded that PEA is transported in to cells both by passive diffusion and by a facilitated transport that is pharmacologically distinguishable from AEA uptake.

L31 ANSWER 7 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2001132951 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10749665
TITLE: The CB1 cannabinoid receptor is coupled to the activation of protein kinase B/Akt.

AUTHOR: Gomez del Pulgar T; Velasco G; Guzman M
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, 28040-Madrid, Spain.
SOURCE: Biochemical journal, (2000 Apr 15) 347 (Pt 2) 369-73. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20021218
Entered Medline: 20010301

AB Cannabinoids exert most of their effects in the central nervous system through the CB(1) cannabinoid receptor. This G-protein-coupled receptor has been shown to be functionally coupled to inhibition of adenylate cyclase, modulation of ion channels and activation of extracellular-signal-regulated kinase. Using Chinese hamster ovary cells stably transfected with the CB(1) receptor cDNA we show here that Delta(9)-**tetrahydrocannabinol** (THC), the major active component of marijuana, induces the activation of protein kinase B/Akt (PKB). This effect of THC was also exerted by the endogenous cannabinoid anandamide and the synthetic cannabinoids CP-55940 and HU-210, and was prevented by the selective CB(1) antagonist SR141716. Pertussis toxin and wortmannin blocked the CB(1) receptor-evoked activation of PKB, pointing to the sequential involvement of a G(i)/G(o) protein and phosphoinositide 3'-kinase. The functionality of the cannabinoid-induced stimulation of PKB was proved by the increased phosphorylation of glycogen synthase kinase-3 serine 21 observed in cannabinoid-**treated** cells and its prevention by SR141716 and wortmannin. Cannabinoids activated PKB in the human **astrocytoma** cell line U373 MG, which expresses the CB(1) receptor, but not in the human promyelocytic cell line HL-60, which expresses the CB(2) receptor. Data indicate that activation of PKB may be responsible for some of the effects of cannabinoids in cells expressing the CB(1) receptor.

L31 ANSWER 8 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2000398263 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10760375
TITLE: Chronic delta-9-**tetrahydrocannabinol** **treatment** increases cAMP levels and cAMP-dependent protein kinase activity in some rat brain regions.
AUTHOR: Rubino T; Vigano' D; Massi P; Spinello M; Zagato E; Giagnoni G; Parolaro D
CORPORATE SOURCE: Institute of Pharmacology, Faculty of Sciences, University of Milan, via Vanvitelli 32/A, 20129, Milan, Italy.
SOURCE: Neuropharmacology, (2000 Apr 27) 39 (7) 1331-6. Journal code: 0236217. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000815

AB When Delta(9)-**tetrahydrocannabinol** (Delta(9)-THC,15 mg/kg) was injected intraperitoneally twice a day for 6 days, tolerance to its analgesic effect appeared to be complete. Chronic exposure to

Delta(9)-THC caused a significant reduction in CB1 receptor binding in all brain areas that contain this receptor. Cannabinoid receptor density was markedly reduced in the cerebellum (52%), hippocampus (40%) and globus pallidum (47%) compared to 30% in the cortex and striatum. Chronic exposure enhanced the cAMP pathway, as shown by the significant increase of cAMP levels and PKA activity in the areas with receptor down-regulation (cerebellum, striatum and cortex). We propose that the increase in cAMP cascade is part of the biochemical basis of cannabinoid tolerance.

L31 ANSWER 9 OF 30 MEDLINE on STN
ACCESSION NUMBER: 1998442860 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9771917
TITLE: Regulation of delta opioid receptors by delta9-**tetrahydrocannabinol** in NG108-15 hybrid cells.
AUTHOR: Di Toro R; Campana G; Sciarretta V; Murari G; Spampinato S
CORPORATE SOURCE: Department of Pharmacology, University of Bologna, Italy.
SOURCE: Life sciences, (1998) 63 (14) PL197-204.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981022

AB In this study we employed the **neuroblastoma** x glioma NG 108-15 cell line as a model for investigating the effects of long-term activation of cannabinoid receptors on delta opioid receptor desensitization, down-regulation and gene expression. Exposure of NG 108-15 cells to (-)-delta9-**tetrahydrocannabinol** (delta9-THC) reduced opioid receptor binding, evaluated in intact cells, by approximately 40-45% in cells exposed for 24 h to 50 and 100 nM delta9-THC and by approximately 25% in cells exposed to 10 nM delta9-THC. Lower doses of delta9-THC (0.1 and 1 nM) or a shorter exposure time to the cannabinoid (6 h) were not effective. Down-regulation of 6 opioid receptors was not observed in cells exposed for 24 h to pertussis toxin (PTX) and then **treated** for 24 h with 100 nM delta9-THC. In cells that were exposed for 24 h to the cannabinoid, the ability of delta9-THC and of the delta opioid receptor agonist [D-Ser2, Leu5, Thr6]enkephalin to inhibit forskolin-stimulated cAMP accumulation was significantly attenuated. Prolonged exposure of NG 108-15 cells to 100 nM delta9-THC produced a significant elevation of steady-state levels of delta opioid receptor mRNA. This effect was not observed in cells **pretreated** with PTX. The selective cannabinoid receptor antagonist SR 141716A blocked the effects elicited by delta9-THC on delta opioid receptor desensitization, down-regulation and gene expression; thus indicating that these are mediated via activation of cannabinoid receptors. These data demonstrate the existence, in NG 108-15 cells, of a complex cross-talk between the cannabinoid and opioid receptors on prolonged exposure to delta9-THC triggered by changes in signaling through Gi and/or G0-coupled receptors.

L31 ANSWER 10 OF 30 MEDLINE on STN
ACCESSION NUMBER: 1998054635 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9392925
TITLE: Intractable nausea and vomiting due to gastrointestinal mucosal metastases relieved by **tetrahydrocannabinol** (dronabinol).
AUTHOR: Gonzalez-Rosales F; Walsh D

CORPORATE SOURCE: Department of Hematology/Oncology, Cleveland Clinic Cancer Center, Cleveland Clinic Foundation, Ohio 44195, USA.
SOURCE: Journal of pain and symptom management, (1997 Nov) 14 (5) 311-4.
Journal code: 8605836. ISSN: 0885-3924.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Nursing Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980114

AB Four years following resection of a Clark's level IV **malignant melanoma**, a 50-year-old man developed widespred metastatic disease involving the liver, bones, brain, gastrointestinal mucosa, and lungs. One week after whole brain radiation **therapy**, he was admitted to the hospital for nausea, vomiting, and pain. He was **treated** with several antiemetic drugs, but it was not until dronabinol was added that the nausea and vomiting stopped. Dronabinol was an effective antiemetic used in combination with prochlorperazine in nausea and vomiting unresponsive to conventional antiemetics.

L31 ANSWER 11 OF 30 MEDLINE on STN
ACCESSION NUMBER: 97272033 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9126878
TITLE: Receptor mediation in cannabinoid stimulated arachidonic acid mobilization and anandamide synthesis.
AUTHOR: Hunter S A; Burstein S H
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Massachusetts Medical School, Worcester 01655-0103, USA.
CONTRACT NUMBER: NIDA 9017 (NIDA)
SOURCE: Life sciences, (1997) 60 (18) 1563-73.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 19970602
Entered Medline: 19970516

AB Numerous reports have suggested that increased synthesis of eicosanoids is a significant effect of cannabinoids in several models including the human. To address the question of receptor mediation in this process we have carried out experiments using oligonucleotides that are antisense to the CB1 and to the CB2 receptors. We have synthesized sense, antisense and random oligonucleotide probes to test for receptor involvement in THC stimulation of arachidonic acid release in three cell lines of both central and peripheral origin. **Treatment** of N18 mouse **neuroblastoma** cells with the CB1 antisense probe, at two concentrations, resulted in a dramatic decrease of THC stimulated arachidonate release while **treatment** with antisense CB2 was less effective. Synthesis of the novel eicosanoid, anandamide, was also reduced by antisense CB1 but not by antisense CB2. Western blot analysis indicated a decreased level of CB1 in CB1 antisense **treated** cells. The CB1 antagonist, SR141716A, was effective in reducing the THC

elevated levels of free arachidonate in these cells in agreement with the antisense data. In the macrophage line, RAW 264.7, we found that while the sense, the random and the CB1 antisense oligonucleotides were ineffective, the CB2 antisense probe gave significant reductions of the THC induced response. The CB2 probe was also effective in reducing the release of arachidonate in WI-38 human lung fibroblasts. These findings support the idea of a receptor mediated process for cannabinoid stimulation of eicosanoid synthesis.

L31 ANSWER 12 OF 30 MEDLINE on STN
ACCESSION NUMBER: 97135521 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8981058
TITLE: Tau protein after delta-9-**tetrahydrocannabinol** in a human **neuroblastoma** cell line.
AUTHOR: Lew G M
CORPORATE SOURCE: Department of Anatomy, College of Human Medicine, Michigan State University, East Lansing 48824, USA.
SOURCE: General pharmacology, (1996 Oct) 27 (7) 1141-3. Journal code: 7602417. ISSN: 0306-3623.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970401

AB 1. A human **neuroblastoma** cell line, SH-SY5Y, was used to determine the effects of delta-9-**tetrahydrocannabinol** (THC) on microtubule-associated tau protein. 2. After 48-hr **treatment**, THC (10(-9) M) decreased 50 kD tau protein in the cytoplasmic (supernatant) fraction, and in the membrane (pellet) fraction the drug (10(-7) M) also decreased 50 kD tau protein. 3. This reduction in tau protein was accompanied by a 27% reduction ($P < 0.05$) in the membrane (pellet) total protein after (10(-7) M) THC and a 28% increase ($P < 0.02$) in cytoplasmic (supernatant) total protein after 10(-9) M THC.

L31 ANSWER 13 OF 30 MEDLINE on STN
ACCESSION NUMBER: 96103206 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8526880
TITLE: Activation of mitogen-activated protein kinases by stimulation of the central cannabinoid receptor CB1.
AUTHOR: Bouaboula M; Poinot-Chazel C; Bourrie B; Canat X; Calandra B; Rinaldi-Carmona M; Le Fur G; Casellas P
CORPORATE SOURCE: Sanofi Recherche, Department of Immunopharmacology, Montpellier, France.
SOURCE: Biochemical journal, (1995 Dec 1) 312 (Pt 2) 637-41. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960219
Last Updated on STN: 20021218
Entered Medline: 19960125

AB The G-protein-coupled central cannabinoid receptor (CB1) has been shown to be functionally associated with several biological responses including inhibition of adenylate cyclase, modulation of ion channels and induction

of the immediate-early gene Krox-24. Using stably transfected Chinese Hamster Ovary cells expressing human CB1 we show here that cannabinoid **treatment** induces both phosphorylation and activation of mitogen-activated protein (MAP) kinases, and that these effects are inhibited by SR 141716A, a selective CB1 antagonist. The two p42 and p44 kDa MAP kinases are activated in a time- and dose-dependent manner. The rank order of potency for the activation of MAP kinases with various cannabinoid agonists is CP-55940 > delta 9-**tetrahydrocannabinol** > WIN 55212.2, in agreement with the pharmacological profile of CB1. The activation of MAP kinases is blocked by pertussis toxin but not by **treatment** with hydrolysis-resistant cyclic AMP analogues. This suggests that the signal transduction pathway between CB1 and MAP kinases involves a pertussis-toxin-sensitive GTP-binding protein and is independent of cyclic AMP metabolism. This coupling of CB1 subtype and mitogenic signal pathway, also observed in the human **astrocytoma** cell line U373 MG, may explain the mechanism of action underlying cannabinoid-induced Krox-24 induction.

L31 ANSWER 14 OF 30 MEDLINE on STN
ACCESSION NUMBER: 95156259 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7853184
TITLE: Low doses of anandamides inhibit pharmacological effects of delta 9-**tetrahydrocannabinol.**
AUTHOR: Fride E; Barg J; Levy R; Saya D; Heldman E; Mechoulam R; Vogel Z
CORPORATE SOURCE: Department of Natural Products, Hebrew University of Jerusalem, Medical Faculty, Israel.
CONTRACT NUMBER: DA6265 (NIDA)
DA6481 (NIDA)
SOURCE: Journal of pharmacology and experimental therapeutics, (1995 Feb) 272 (2) 699-707.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 20000303
Entered Medline: 19950315

AB It has been shown previously that the endogenous cannabinoid receptor ligand arachidonylethanolamide (anandamide 20:4, n-6) induces in vivo and in vivo effects typical of a cannabinoid partial agonist. We now report that the synthetic docosahexaenylethanolamide (anandamide 22:6, n-3) shows similar activities. In addition we show that these two anandamides, under certain experimental conditions, antagonize the effects of delta 9-THC both in vivo and in vitro. Thus a significant decrease in the potency of delta 9-THC-induced inhibition of adenylate cyclase was observed in N18TG2 **neuroblastoma** cells that were **pretreated** with low concentrations of anandamides. At these low concentrations of anandamides had no effect when applied alone. In vivo, Sabra or ICR mice were subjected to a tetrad of tests, designed to detect cannabinoid-induced effects. Mice **pretreated** (i.p.) with 10 mg/kg of delta 9-THC received injections with anandamides. Only low doses (0.0001-0.1 mg/kg) of the anandamides, which had no effects when administered alone, partially or fully inhibited the THC-induced effects. These findings suggest that the inhibition of delta 9-THC-induced effects by low doses of anandamides may be due to partial agonistic effects of these materials. It is possible that low doses of the anandamides are capable of activating

a Gs protein mediated signaling pathway, or may cause an allosteric modulation of the cannabinoid receptor.

L31 ANSWER 15 OF 30 MEDLINE on STN
ACCESSION NUMBER: 92237261 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1315042
TITLE: Cannabinoids inhibit N-type calcium channels in **neuroblastoma**-glioma cells.
AUTHOR: Mackie K; Hille B
CORPORATE SOURCE: Department of Anesthesiology, University of Washington School of Medicine, Seattle 98195.
CONTRACT NUMBER: GM07604-12 (NIGMS)
NS08174 (NINDS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1992 May 1) 89 (9) 3825-9.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920612
Last Updated on STN: 20021218
Entered Medline: 19920528

AB The psychoactive properties of Cannabis sativa and its major biologically active constituent, delta 9-**tetrahydrocannabinol**, have been known for years. The recent identification and cloning of a specific cannabinoid receptor suggest that cannabinoids mimic endogenous compounds affecting neural signals for mood, memory, movement, and pain. Using whole-cell voltage clamp and the cannabinomimetic aminoalkylindole WIN 55,212-2, we have found that cannabinoid receptor activation reduces the amplitude of voltage-gated calcium currents in the **neuroblastoma** -glioma cell line NG108-15. The inhibition is potent, being half-maximal at less than 10 nM, and reversible. The inactive enantiomer, WIN 55,212-3, does not reduce calcium currents even at 1 microM. Of the several types of calcium currents in NG108-15 cells, cannabinoids predominantly inhibit an omega-conotoxin-sensitive, high-voltage-activated calcium current. Inhibition was blocked by incubation with pertussis toxin but was not altered by prior **treatment** with hydrolysis-resistant cAMP analogues together with a phosphodiesterase inhibitor, suggesting that the transduction pathway between the cannabinoid receptor and calcium channel involves a pertussis toxin-sensitive GTP-binding protein and is independent of cAMP metabolism. However, the development of inhibition is considerably slower than a pharmacologically similar pathway used by an alpha 2-adrenergic receptor in these cells. Our results suggest that inhibition of N-type calcium channels, which could decrease excitability and neurotransmitter release, may underlie some of the psychoactive effects of cannabinoids.

L31 ANSWER 16 OF 30 MEDLINE on STN
ACCESSION NUMBER: 91078286 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2175265
TITLE: Delta-9-**tetrahydrocannabinol** shows antispastic and analgesic effects in a single case double-blind trial.
AUTHOR: Maurer M; Henn V; Dittrich A; Hofmann A
CORPORATE SOURCE: PSIN - Psychologisches Institut fur Beratung und Forschung, Zurich, Switzerland.
SOURCE: European archives of psychiatry and clinical neuroscience, (1990) 240 (1) 1-4.

Journal code: 9103030. ISSN: 0940-1334.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CASE REPORTS)
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19990129
Entered Medline: 19910128

AB A double-blind study was performed comparing 5 mg delta-9-**tetrahydrocannabinol** (THC) p.o., 50 mg codeine p.o., and placebo in a patient with spasticity and pain due to spinal cord injury. The three conditions were applied 18 times each in a randomized and balanced order. Delta-9-THC and codeine both had an analgesic effect in comparison with placebo. Only delta-9-THC showed a significant beneficial effect on spasticity. In the dosage of THC used no altered consciousness occurred.

L31 ANSWER 17 OF 30 MEDLINE on STN
ACCESSION NUMBER: 89293673 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2855242
TITLE: Regulation of adenylate cyclase by chronic exposure to cannabimimetic drugs.
AUTHOR: Dill J A; Howlett A C
CORPORATE SOURCE: Department of Pharmacology, St. Louis University School of Medicine, Missouri.
CONTRACT NUMBER: DA03690 (NIDA)
NS00868 (NINDS)
SOURCE: Journal of pharmacology and experimental therapeutics, (1988 Mar) 244 (3) 1157-63.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19980206
Entered Medline: 19890810

AB Previous studies in this laboratory have demonstrated that a cloned **neuroblastoma** cell line (N18TG2) responds to delta 9-**tetrahydrocannabinol** (THC), the major psychoactive product of marihuana, with an attenuation of cyclic AMP accumulation that results from an inhibition of adenylate cyclase. The requirement for the Gi regulatory protein, stereoselectivity, pharmacologic specificity and cell selectivity of this response suggest that a receptor for cannabimimetic compounds may be associated with adenylate cyclase in the **neuroblastoma** cell. Presented here is a comprehensive investigation of cellular effects of chronic exposure to cannabimimetic agents. Short-term exposure to either delta 9-THC or the more potent nantradol analog, desacetyllevonantradol (DALN), at doses up to 100 microM did not compromise the plating efficiency of the cells. Cells that were exposed to 1 microM delta 9-THC (maximally effective for inhibiting cyclic AMP production) for 24 hr in a serum-free medium were shown to accumulate the drug but not to metabolize it. Exposure to 10 microM delta 9-THC or DALN for up to 48 hr failed to significantly affect cell growth rate or protein content per cell. The gross morphology of cannabinoid-

treated cells was not altered at the light or the electron microscope level. The cellular organelles and membranes appeared intact, with no remarkable differences from control cells. The inhibition of cyclic AMP accumulation in response to cannabimimetic drugs was diminished in cells **treated** with delta 9-THC or DALN for 24 hr. This desensitization was homologous because both delta 9-THC and DALN responses were attenuated after exposure to either cannabimimetic drug.(ABSTRACT TRUNCATED AT 250 WORDS)

L31 ANSWER 18 OF 30 MEDLINE on STN
ACCESSION NUMBER: 88023358 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2821958
TITLE: Interaction of delta-9-**tetrahydrocannabinol** with rat B103 **neuroblastoma** cells.
AUTHOR: Cabral G A; McNerney P J; Mishkin E M
CORPORATE SOURCE: Department of Microbiology and Immunology, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298.
CONTRACT NUMBER: 2S07 RR05724 (NCRR)
2S07 RRO5430 (NCRR)
RO1 DAP 3647 (NIDA)
+
SOURCE: Archives of toxicology, (1987 Aug) 60 (6) 438-49.
Journal code: 0417615. ISSN: 0340-5761.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198711
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19871112

AB The effect of delta-9-**tetrahydrocannabinol** (delta-9-THC) on the growth kinetics and morphology of rat B103 **neuroblastoma** cells was assessed. Delta-9-THC in doses ranging from 10(-4) to 10(-7) M inhibited cellular growth in a dose-dependent fashion as evidenced by delay in doubling time, decrease in saturation density, and decrease in efficiency of plating. The inhibition in cellular growth was paralleled by dose-related alterations in cell morphology. Modifications included rounding of cells, retraction of neurites, blebbing of the cell surface, and exfoliation of the plasma membrane. Cytoplasmic alterations included distension of the endoplasmic reticulum, Golgi apparatus, and perinuclear space, and macrovacuolization. Intracytoplasmic laminated inclusions and vesicular clusters were suggestive of membrane repair in drug-**treated** cells. These morphological changes were accompanied by cytoskeletal rearrangement in the absence of significant alteration in the concentration of total cytoskeletal protein. Autoradiographic examination of the intracellular fate of 3H-delta-9-THC demonstrated that the drug was confined to the cytoplasmic compartment and often associated with macrovacuoles. These results suggest that delta-9-THC interacts with cellular membranes, thereby altering **neuroblastoma** cell growth and behavior.

L31 ANSWER 19 OF 30 MEDLINE on STN
ACCESSION NUMBER: 86146567 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2869405
TITLE: Involvement of Gi in the inhibition of adenylate cyclase by cannabimimetic drugs.
AUTHOR: Howlett A C; Qualy J M; Khachatrian L L

CONTRACT NUMBER: DA 03690 (NIDA)
NS 00868 (NINDS)
NS 16513 (NINDS)
SOURCE: Molecular pharmacology, (1986 Mar) 29 (3) 307-13.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 20021218
Entered Medline: 19860424

AB The cellular mechanism of action of the cannabimimetic drugs is examined using cultured cells. In membranes from N18TG2 **neuroblastoma** cells and the **neuroblastoma** X glioma hybrid cells, NG108-15, the psychoactive cannabinoid drugs and their nantradol analogs could inhibit adenylate cyclase activity. This response was not observed in either the soluble adenylate cyclase from rat sperm or membrane-bound adenylate cyclases from C6 glioma or S49 lymphoma cells. This cellular selectivity provides further evidence for the existence of specific receptors for the cannabimimetic compounds. Receptor-mediated inhibition of adenylate cyclase requires the presence of a guanine nucleotide-binding protein complex, Gi. Gi can be functionally inactivated as a result of an ADP-ribosylation modification catalyzed by pertussis toxin. The present study demonstrates that pertussis toxin **treatment** of cells abolished the cannabimimetic response in intact cells and in membranes derived therefrom. The action of pertussis toxin required NAD+ as substrate for in vitro modification of **neuroblastoma** membranes. Furthermore, pertussis toxin was able to catalyze the labeling of a **neuroblastoma** membrane protein in vitro using [32P] NAD+ under conditions similar to those by which attenuation of the cannabimimetic inhibition of adenylate cyclase could be demonstrated. This evidence demonstrates the requirement for a functional Gi in the action of cannabimimetic drugs.

L31 ANSWER 20 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:250718 BIOSIS
DOCUMENT NUMBER: PREV200400251435
TITLE: Oleamide is a selective endogenous agonist of rat and human CB1 cannabinoid receptors.
AUTHOR(S): Leggett, James D. [Reprint Author]; Aspley, S.; Beckett, S. R. G.; D'Antona, A. M.; Kendall, D. A.
CORPORATE SOURCE: School of Biomedical Sciences, Medical School, University of Nottingham, Queens Medical Centre, Nottingham, NG7 2UH, UK
mbxjdl@nottingham.ac.uk
SOURCE: British Journal of Pharmacology, (January 2004) Vol. 141, No. 2, pp. 253-262. print.
ISSN: 0007-1188 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 May 2004
Last Updated on STN: 12 May 2004

AB 1 The ability of the endogenous fatty acid amide, cis-oleamide (ODA), to bind to and activate cannabinoid CB1 and CB2 receptors was investigated. 2 ODA competitively inhibited binding of the nonselective cannabinoid agonist (3H)CP55,940 and the selective CB1 antagonist (3H)SR141716A to rat

whole-brain membranes with Ki values of 1.14 muM (0.52-2.53 muM, Hill slope=0.80, n=6) and 2.63 muM (0.62-11.20 muM, Hill slope=0.92, n=4), respectively. AEA inhibited (3H)CP55,940 binding in rat whole-brain membranes with a Ki of 428 nM (346-510 nM, Hill slope=-1.33, n=3). 3 ODA competitively inhibited (3H)CP55,940 binding in human CB1 (hCB1) cell membranes with a Ki value of 8.13 muM (4.97-13.32 muM, n=2). In human CB2 transfected (hCB2) HEK-293T cell membranes, 100 muM ODA produced only a partial (42.5+-7%) inhibition of (3H)CP55,940 binding. 4 ODA stimulated (35S)GTPgammaS binding in a concentration-dependent manner (EC50=1.64 muM (0.29-9.32 muM), R2=0.99, n=4-9), with maximal stimulation of 188+-9% of basal at 100 muM. AEA stimulated (35S)GTPgammaS binding with an EC50 of 10.43 muM (4.45-24.42 muM, R2=1.00, n=3, 195+-4% of basal at 300 muM). Trans-oleamide (trans-ODA) failed to significantly stimulate (35S)GTPgammaS binding at concentrations up to 100 muM. 5 ODA (10 muM)-stimulated (35S)GTPgammaS binding was reversed by the selective CB1 antagonist SR141716A (IC50=2.11 nM (0.32-13.77 nM), R2=1.00, n=6). 6 The anatomical distribution of ODA-stimulated (35S)GTPgammaS binding in rat brain sections was indistinguishable from that of HU210. Increases of similar magnitude were observed due to both agonists in the striatum, cortex, hippocampus and cerebellum. 7 ODA (10 muM) significantly inhibited forskolin-stimulated cyclic AMP (cAMP) accumulation in mouse **neuroblastoma** N1E 115 cells (P=0.02, n=11). ODA-mediated inhibition was completely reversed by 1 muM SR141716A (P<0.001, n=11) and was also reversed by **pretreatment** with 300 ng ml-1 pertussis toxin (P<0.001, n=6). 8 These data demonstrate that ODA is a full cannabinoid CB1 receptor agonist. Therefore, in addition to allosteric modulation of other receptors and possible entourage effects due to fatty acid amide hydrolase inhibition, the effects of ODA may be mediated directly via the CB1 receptor.

L31 ANSWER 21 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:499117 BIOSIS
DOCUMENT NUMBER: PREV200300501252
TITLE: The CB1 cannabinoid receptor agonist, HU-210, reduces levodopa-induced rotations in 6-hydroxydopamine-lesioned rats.
AUTHOR(S): Gilgun-Sherki, Yossi; Melamed, Eldad; Mechoulam, Raphael; Offen, Daniel [Reprint Author]
CORPORATE SOURCE: Felsenstein Medical Research Center, Tel Aviv University, and Rabin Medical Center, Beilinson Campus, Petah Tikva, 49100, Israel
doffen@post.tau.ac.il
SOURCE: Pharmacology & Toxicology, (August 2003) Vol. 93, No. 2, pp. 66-70. print.
CODEN: PHTOEH. ISSN: 0901-9928.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003

AB Parkinson's disease is a chronic neurodegenerative disease of the extrapyramidal system associated with dopaminergic neuronal loss in the basal ganglia. However, several other neurotransmitters, such as serotonin, gamma-amino-butyric acid and glutamate, are also related to the symptoms of Parkinson's disease patients and their response to levodopa **treatment.** The co-expression of cannabinoid and dopamine receptors in the basal ganglia suggests a potential role for endocannabinoids in the control of voluntary movement in Parkinson's disease. In the present study we **treated** unilaterally

2,4,5-trihydroxyphenethylamine (6-hydroxydopamine)-lesioned rats with the enantiomers of the synthetic cannabinoid 7-hydroxy-DELTA6-**tetrahydrocannabinol** 1,1-dimethylheptyl. **Treatment** with its (-)- (3R, 4R) enantiomer (code-name HU-210), a potent cannabinoid receptor type 1 agonist, reduced the rotations induced by levodopa/carbidopa or apomorphine by 34% and 44%, respectively. In contrast, **treatment** with the (+)- (3S, 4S) enantiomer (code-name HU-211), an N-methyl-D-aspartate antagonist, as well as the psychotropically inactive cannabis constituent: **cannabidiol** and its primary metabolite, 7-**hydroxycannabinol**, did not show any reduction of rotational behavior. Our results indicate that activation of the CB1 stimulates the dopaminergic system ipsilaterally to the lesion, and may have implications in the **treatment** of Parkinson's disease.

L31 ANSWER 22 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:316901 BIOSIS
DOCUMENT NUMBER: PREV200300316901
TITLE: The endocannabinoid system as a target for the development of new drugs for cancer **therapy.**
Original Title: Il sistema endocannabinoide quale bersaglio di terapie anti-tumorali. Conoscenze attuali e prospettive..
AUTHOR(S): Bifulco, Maurizio [Reprint Author]; Di Marzo, Vincenzo
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Salerno, Via Ponte Don Melillo, 84084, Fisciano (Salerno), Italy
maubiful@unina.it
SOURCE: Recenti Progressi in Medicina, (Maggio 2003) Vol. 94, No. 5, pp. 194-198. print.
CODEN: RPMDAN. ISSN: 0034-1193.
DOCUMENT TYPE: Article
LANGUAGE: Italian
ENTRY DATE: Entered STN: 9 Jul 2003
Last Updated on STN: 9 Jul 2003

AB Studies on the main bioactive components of Cannabis sativa, the cannabinoids, and particularly DELTA9-**tetrahydrocannabinol** (THC), led to the discovery of a new endogenous signalling system that controls several physiological and pathological conditions: the endocannabinoid system. This comprises the cannabinoid receptors, their endogenous agonists - the endocannabinoids - and proteins for endocannabinoid biosynthesis and inactivation. Recently, evidence has accumulated indicating that stimulation of cannabinoid receptors by either THC or the endocannabinoids influence the intracellular events controlling the proliferation and apoptosis of numerous types of cancer cells, thereby leading to anti-tumour effects both in vitro and in vivo. This evidence is reviewed here and suggests that future anti-cancer **therapy** might be developed from our knowledge of how the endocannabinoid system controls the growth and metastasis of malignant cells.

L31 ANSWER 23 OF 30 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:450141 BIOSIS
DOCUMENT NUMBER: PREV200000450141 Inventor
TITLE: Cannabinoid **therapy** against brain tumors.
AUTHOR(S): Guzman, M. [Reprint author]
CORPORATE SOURCE: Complutense University, 28040, Madrid, Spain
SOURCE: Biomedicine and Pharmacotherapy, (August, 2000) Vol. 54,

No. 7, pp. 415. print.
CODEN: BIPHEX. ISSN: 0753-3322.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

L31 ANSWER 24 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2005282881 EMBASE
TITLE: Targeted molecular **therapy** of malignant gliomas.
AUTHOR: Kesari S.; Ramakrishna N.; Sauvageot C.; Stiles C.D.; Wen P.Y.
CORPORATE SOURCE: Dr. P.Y. Wen, Center For Neuro-Oncology, Dana Farber/Brigham and Women's Cancer Center, 44 Binney Street, Boston, MA 02115, United States. pwen@partners.org
SOURCE: Current Neurology and Neuroscience Reports, (2005) Vol. 5, No. 3, pp. 186-197.
Refs: 112
ISSN: 1528-4042 CODEN: CNNRBS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050714
Last Updated on STN: 20050714

AB Malignant gliomas are the most common form of primary brain tumors in adults. Despite advances in diagnosis and standard **therapies** such as surgery, radiation, and **chemotherapy**, the prognosis remains poor. Recent scientific advances have enhanced our understanding of the biology of gliomas and the role of tyrosine kinase receptors and signal transduction pathways in tumor initiation and maintenance, such as the epidermal growth factor receptors, platelet-derived growth factor receptors, vascular endothelial growth factor receptors, and the Ras/Raf/mitogen-activated protein (MAP)-kinase and phosphatidylinositol-3 kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) pathways. Novel targeted drugs such as small molecular inhibitors of these receptors and signaling pathways are showing some activity in initial studies. As we learn more about these drugs and how to optimize their use as single agents and in combination with radiation, **chemotherapy**, and other targeted molecular agents, they will likely play an increasing role in the management of this devastating disease. This review summarizes the current results with targeted molecular agents in malignant gliomas and strategies under evaluation to increase their effectiveness. Copyright .COPYRGT. 2005 by Current Science Inc.

L31 ANSWER 25 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004389354 EMBASE
TITLE: Arachidonylethanolamide induces apoptosis of human glioma cells through vanilloid receptor-1.
AUTHOR: Contassot E.; Wilmotte R.; Tenan M.; Belkouch M.-C.; Schnuriger V.; De Tribolet N.; Bourkhardt K.; Dietrich P.-Y.
CORPORATE SOURCE: Dr. P.-Y. Dietrich, Laboratory of Tumor Immunology,

Oncology Division, University Hospital, Rue Micheli-du-Crest 24, 1211 Geneva 14, Switzerland. pierre-yves.dietrich@hcuge.ch
SOURCE: Journal of Neuropathology and Experimental Neurology, (2004) Vol. 63, No. 9, pp. 956-963.
Refs: 56
ISSN: 0022-3069 CODEN: JNENAD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040930
Last Updated on STN: 20040930
AB The anti-tumor properties of cannabinoids have recently been evidenced, mainly with Δ(9)- **tetrahydrocannabinol** (THC). However, the clinical application of this drug is limited by possible undesirable side effects due to a broad expression of cannabinoid receptors (CB1 and CB2). An attractive field of research therefore is to identify molecules with more selective tumor targeting. This is particularly important for malignant gliomas, considering their poor prognosis and their location in the brain. Here we investigated whether the most potent endogenous cannabinoid, arachidonylethanolamide (AEA), could be a candidate. We observed that AEA induced apoptosis in long-term and recently established glioma cell lines via aberrantly expressed vanilloid receptor-1 (VR1). In contrast with their role in THC-mediated death, both CB1 and CB2 partially protected glioma against AEA-induced apoptosis. These data show that the selective targeting of VR1 by AEA or more stable analogues is an attractive research area for the **treatment** of glioma.

L31 ANSWER 26 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003513532 EMBASE
TITLE: Cannabinoid receptor systems: **Therapeutic** targets for tumour intervention.
AUTHOR: Jones S.; Howl J.
CORPORATE SOURCE: Dr. J. Howl, Molecular Pharmacology Group, School of Applied Sciences, University of Wolverhampton, Wulfruna Street, Wolverhampton WV1 1SB, United Kingdom. J.Howl@wlv.ac.uk
SOURCE: Expert Opinion on Therapeutic Targets, (2003) Vol. 7, No. 6, pp. 749-758.
Refs: 101
ISSN: 1472-8222 CODEN: EOTTAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040105
Last Updated on STN: 20040105
AB The past decade has witnessed a rapid expansion of our understanding of the biological roles of cannabinoids and their cognate receptors. It is

now certain that Δ(9)- **tetrahydrocannabinol**, the principle psychoactive component of the Cannabis sativa plant, binds and activates membrane receptors of the 7-transmembrane domain, G-protein-coupled superfamily. Several putative endocannabinoids have since been identified, including anandamide, 2-arachidonyl glycerol and noladin ether. Synthesis of numerous cannabinomimetics has also greatly expanded the repertoire of cannabinoid receptor ligands with the pharmacodynamic properties of agonists, antagonists and inverse agonists. Collectively, these ligands have proven to be powerful tools both for the molecular characterisation of cannabinoid receptors and the delineation of their intrinsic signalling pathways. Much of our understanding of the signalling mechanisms activated by cannabinoids is derived from studies of receptors expressed by tumour cells; hence, this review provides a succinct summary of the molecular pharmacology of cannabinoid receptors and their roles in tumour cell biology. Moreover, there is now a genuine expectation that the manipulation of cannabinoid receptor systems may have **therapeutic** potential for a diverse range of human diseases. Thus, this review also summarises the demonstrated antitumour actions of cannabinoids and indicates possible avenues for the future development of cannabinoids as antitumour agents.

L31 ANSWER 27 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000356698 EMBASE
TITLE: Recent advances in cannabinoid receptor agonists and antagonists.
AUTHOR: Goya P.; Jagerovic N.
CORPORATE SOURCE: P. Goya, Instituto de Quimica Medica, CSIC, Juan de la Cierva 3, E-28006 Madrid, Spain. iqmg310@iqm.csic.es
SOURCE: Expert Opinion on Therapeutic Patents, (2000) Vol. 10, No. 10, pp. 1529-1538.
Refs: 40
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20001026
Last Updated on STN: 20001026

AB This review is an overview of the recent advances in cannabinoid chemistry with a special emphasis on the patent literature. The term cannabinoid includes analogues of the natural components of cannabis, endocannabinoids and a wide array of chemical structures such as 1,5-diarylpyrazoles, indoles, quinolines and arylsulphonamide derivatives capable of acting as cannabinoid receptor agonists and antagonists. These receptors, discovered in the early nineties, seem to be involved in different biochemical processes and thus represent interesting **therapeutic** targets for drug research.

L31 ANSWER 28 OF 30 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000103762 EMBASE
TITLE: Cannabis may be useful for brain tumours and MS, researchers say.

SOURCE: Life Sciences, (28 Aug 1998) Vol. 63, No. 14, pp. PL197-PL204.
Refs: 27
ISSN: 0024-3205 CODEN: LIFSAK
PUBLISHER IDENT.: S 0024-3205(98)00390-7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990819
Last Updated on STN: 19990819

AB In this study we employed the **neuroblastoma** x glioma NG 108-15 cell line as a model for investigating the effects of long-term activation of cannabinoid receptors on δ opioid receptor desensitization, down-regulation and gene expression. Exposure of NG 108-15 cells to (-)-Δ9- **tetrahydrocannabinol** (Δ9-THC) reduced opioid receptor binding, evaluated in intact cells, by .simeq. 40 - 45% in cells exposed for 24 h to 50 and 100 nM Δ9- THC and by .simeq. 25 % in cells exposed to 10 nM Δ9-THC. Lower doses of Δ9- THC (0.1 and 1 nM) or a shorter exposure time to the cannabinoid (6 h) were not effective. Down-regulation of δ opioid receptors was not observed in cells exposed for 24 h to pertussis toxin (PTX) and then **treated** for 24 h with 100 nM Δ9-THC. In cells that were exposed for 24 h to the cannabinoid, the ability of Δ9-THC and of the δ opioid receptor agonist [D-Ser2, Leu5, Thr6]enkephalin to inhibit forskolin-stimulated cAMP accumulation was significantly attenuated. Prolonged exposure of NG 108-15 cells to 100 nM Δ9-THC produced a significant elevation of steady-state levels of δ opioid receptor mRNA. This effect was not observed in cells **pretreated** with PTX. The selective cannabinoid receptor antagonist SR 141716A blocked the effects elicited by Δ9-THC on δ opioid receptor desensitization, down-regulation and gene expression; thus indicating that these are mediated via activation of cannabinoid receptors. These data demonstrate the existence, in NG 108-15 cells, of a complex cross-talk between the cannabinoid and opioid receptors on prolonged exposure to Δ9-THC triggered by changes in signaling through G(i) and/or GO-coupled receptors.

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=> d que stat l36
L20           1 SEA FILE=REGISTRY ABB=ON  Δ8-TETRAHYDROCANNABINOL/CN
L21           2 SEA FILE=REGISTRY ABB=ON  (CANNABINOL OR CANNABIDIOL)/CN
L22           3 SEA FILE=REGISTRY ABB=ON  L20 OR L21
L23        5906 SEA FILE=HCAPLUS ABB=ON  L22 OR (Δ8-TETRAHYDROCANNABINOL?
                OR ?CANNABINOL? OR ?CANNABIDIOL?)
L24          68 SEA FILE=HCAPLUS ABB=ON  L23 AND (?BLASTOMA? OR ?EPITHELOMA?
                OR ?GERMINOMA? OR ?CARCINOMA? OR ?ASTROCYTOMA? OR ?EPENDYMOMA?
                OR ?OLIGODENROGLIOMA? OR ?OLIGODENDROGLIOMA? OR ?NEUROEPITHELOM
                A? OR ?NEUROECTODERM?(W)(?TUMOR? OR ?TUMOUR?) OR ?MENINGIOMA?
                OR ?SARCOMA? OR ?MELANOMA? OR ?SCHWANOMA?)
L25          29 SEA FILE=HCAPLUS ABB=ON  L24 AND (?THERAP? OR ?TREAT? OR
                ?CURE? OR ?IMPROV?)
L27         150 SEA L25
L32          60 SEA FILE=USPATFULL ABB=ON  L27 AND (?GLIOBLASTOMA? OR ?MEDUL?(W
                )?EPITHELOMA? OR ?MEDULOBLASTOMA? OR ?NEUROBLASTOMA? OR
                ?GERMINOMA? OR ?EMBROYOCARCINOMA? OR ?ASTROCYTOMA? OR ?ASTROBLA
                STOMA? OR ?EPENDYMOMA? OR ?OLIGODENROGLIOMA? OR ?PLEXOCARCINOMA
                ? OR ?NEUROEPITHELOMA? OR ?PINEOBLASTOMA? OR ?EPANDIMOBLASTOMA?
                )
L33          32 SEA FILE=USPATFULL ABB=ON  L27 AND (?NEUROECTODERM?(W)(?TUMOR?
                OR ?TUMOUR?) OR ?MALIGN?(W)(?MENINGIOMA? OR ?MELANOMA? OR
                ?SCHWANOMA?) OR ?CHONDROSARCOMA? OR ?MENINGEAL?(W)?SARCOM?)
L34          63 SEA FILE=USPATFULL ABB=ON  L32 OR L33
L35          51 SEA FILE=USPATFULL ABB=ON  L34 AND (PRD<20030825 OR PD<20030825
                )
L36          32 SEA FILE=USPATFULL ABB=ON  L35 AND ?TREAT?(5A)?THERAP?

=> d ibib abs l36 1-32

L36  ANSWER 1 OF 32  USPATFULL on STN
ACCESSION NUMBER:        2005:124949  USPATFULL
TITLE:                   Diphenylethylene compounds and uses thereof
INVENTOR(S):             Muller, George W., Bridgewater, NJ, UNITED STATES
                         Payvandi, Faribourz, Belle Mead, NJ, UNITED STATES
                         Zhang, Ling H., Parsippany, NJ, UNITED STATES
                         Robarge, Michael J., Burton, OH, UNITED STATES
                         Chen, Roger, Edison, NJ, UNITED STATES
                         Man, Hon-Wah, Princeton, NJ, UNITED STATES
                         Ruchelman, Alexander L., Robbinsville, NJ, UNITED
                         STATES
PATENT ASSIGNEE(S):      Celgene Corporation (U.S. corporation)

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2005107339      A1   20050519
APPLICATION INFO.:       US 2004-934974     A1   20040903  (10)
RELATED APPLN. INFO.:    Continuation-in-part of Ser. No. US 2004-794931, filed
                         on 5 Mar 2004, PENDING

                                NUMBER         DATE
                         ------------------ --------
PRIORITY INFORMATION:    US 2003-452460P    20030305 (60)           <--
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017, US
NUMBER OF CLAIMS:        30
EXEMPLARY CLAIM:         1
LINE COUNT:              10022
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to Diphenylethylene Compounds and compositions comprising a Diphenylethylene Compound. The present invention also relates to methods for preventing or **treating** various diseases and disorders by administering to a subject in need thereof one or more Diphenylethylene Compounds. In particular, the invention relates to methods for preventing or **treating** cancer or an inflammatory disorder by administering to a subject in need thereof one or more Diphenylethylene Compounds. The present invention further relates to articles of manufacture and kits comprising one or more Diphenylethylene Compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 2 OF 32 USPATFULL on STN

ACCESSION NUMBER:	2005:124277 USPATFULL		
TITLE:	Binding polypeptides with restricted diversity sequences		
INVENTOR(S):	Fellouse, Frederic A., San Francisco, CA, UNITED STATES Sidhu, Sachdev, San Francisco, CA, UNITED STATES		
PATENT ASSIGNEE(S):	GENENTECH, INC (U.S. corporation)		

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005106667	A1	20050519	
APPLICATION INFO.:	US 2004-901011	A1	20040728	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-491877P	20030801	(60) <--

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA, 94080, US
NUMBER OF CLAIMS:	29
EXEMPLARY CLAIM:	1-25
NUMBER OF DRAWINGS:	30 Drawing Page(s)
LINE COUNT:	6147

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides variant CDRs comprising highly restricted amino acid sequence diversity. These polypeptides provide a flexible and simple source of sequence diversity that can be used as a source for identifying novel antigen binding polypeptides. The invention also provides these polypeptides as fusion polypeptides to heterologous polypeptides such as at least a portion of phage or viral coat proteins, tags and linkers. Libraries comprising a plurality of these polypeptides are also provided. In addition, methods of and compositions for generating and using these polypeptides and libraries are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 3 OF 32 USPATFULL on STN

ACCESSION NUMBER:	2005:112172 USPATFULL
TITLE:	Compositions for manipulating the lifespan and stress response of cells and organisms
INVENTOR(S):	Sinclair, David A., West Roxbury, MA, UNITED STATES
PATENT ASSIGNEE(S):	President and Fellows of Harvard College, Cambridge, MA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005096256	A1	20050505	
APPLICATION INFO.:	US 2004-884022	A1	20040701	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-483949P	20030701 (60)	<--
	US 2003-532158P	20031223 (60)	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FOLEY HOAG, LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BLVD, BOSTON, MA, 02110, US
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 42 Drawing Page(s)
LINE COUNT: 6583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided herein are methods and compositions for modulating the activity of sirtuin deacetylase protein family members; p53 activity; apoptosis; lifespan and sensitivity to stress of cells and organisms. Exemplary methods comprise contacting a cell with an activating compound, such as a flavone, stilbene, flavanone, isoflavone, catechin, chalcone, tannin or anthocyanidin; or an inhibitory compound, such as a sphingolipid, e.g., sphingosine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 4 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2005:105576 USPATFULL
TITLE: Trp-p8 active compounds and **therapeutic treatment** methods
INVENTOR(S): Reynolds, Mark, Millbrae, CA, UNITED STATES
Polakis, Paul, Burlingame, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005090514	A1	20050428	
APPLICATION INFO.:	US 2004-884379	A1	20040702	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-484526P	20030702 (60)	<--
	US 2003-491616P	20030731 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Merchant & Gould P.C., P.O. Box 2903, Minneapolis, MN, 55402-0903, US
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1800
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of the disclosure provide compositions, which are effective for prophylaxis and **treatment** of diseases or disorders, such as cell-proliferation, angiogenesis, or apoptosis mediated diseases. The disclosure encompasses compounds, analogs, prodrugs, metabolites, and pharmaceutically acceptable salts thereof, pharmaceutical compositions, and methods for prophylaxis and **treatment** of diseases and

other maladies or conditions involving cancer, tumors, and like conditions. The disclosure also provides **therapeutic** methods including the administration of an effective amount of a compound of the disclosure.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 5 OF 32 USPATFULL on STN

ACCESSION NUMBER:	2005:63608 USPATFULL
TITLE:	Use of glutamate antagonists for the **treatment** of cancer
INVENTOR(S):	Ikonomidou, Hrissanthi, Berlin, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005054650	A1	20050310
APPLICATION INFO.:	US 2004-912175	A1	20040806 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-830354, filed on 25 Apr 2001, GRANTED, Pat. No. US 6797692 A 371 of International Ser. No. WO 1999-EP8004, filed on 22 Oct 1999, UNKNOWN

	NUMBER	DATE	
PRIORITY INFORMATION:	DE 1998-250380	19981028	<--

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
NUMBER OF CLAIMS:	8
EXEMPLARY CLAIM:	CLM-01-37
NUMBER OF DRAWINGS:	5 Drawing Page(s)
LINE COUNT:	1004

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods for **treating** cancer by administering an inhibitor of the interaction of glutamate with the NMDA/glycine/polyamine receptor/ion channel complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 6 OF 32 USPATFULL on STN

ACCESSION NUMBER:	2005:63577 USPATFULL
TITLE:	Use of glutamate antagonists for the **treatment** of cancer
INVENTOR(S):	Ikonomidou, Hrissanthi, Berlin, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005054619	A1	20050310
APPLICATION INFO.:	US 2004-912159	A1	20040806 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-830354, filed on 25 Apr 2001, GRANTED, Pat. No. US 6797692 A 371 of International Ser. No. WO 1999-EP8004, filed on 22 Oct 1999, UNKNOWN

	NUMBER	DATE

PRIORITY INFORMATION: DE 1998-250380 19981028 <--
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: CLM-01-37
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 760
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods for **treating** cancer by administering an inhibitor of the interaction of glutamate with the KA receptor complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 7 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2005:50527 USPATFULL
TITLE: Pharmaceutical composition for the prevention and **treatment** of addiction in a mammal
INVENTOR(S): Coe, Jotham Wadsworth, Niantic, CT, UNITED STATES
Iredale, Philip A., Clinton, CT, UNITED STATES
McHardy, Stanton Furst, Coventry, RI, UNITED STATES
McLean, Stafford, Stonington, CT, UNITED STATES
PATENT ASSIGNEE(S): Pfizer Inc (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005043327	A1	20050224	
APPLICATION INFO.:	US 2004-870209	A1	20040617	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-496803P	20030821 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 2088
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pharmaceutical compositions are disclosed for the **treatment** of alcohol or cocaine dependence or addiction, tobacco dependence or addiction, reduction of alcohol withdrawal symptoms or aiding in the cessation or lessening of alcohol use or substance abuse or other behavioral dependencies including gambling. The pharmaceutical compositions are comprised of a **therapeutically** effective combination of an opioid receptor antagonist and a CB-1 receptor antagonist and a pharmaceutically acceptable carrier. The method of using these compounds is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 8 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2005:50478 USPATFULL
TITLE: Hydroxyl compounds and compositions for cholesterol management and related uses
INVENTOR(S): Dasseux, Jean-Louis Henri, Brighton, MI, UNITED STATES
Oniciu, Carmen Daniela, Ann Arbor, MI, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005043278	A1	20050224	
APPLICATION INFO.:	US 2003-743470	A1	20031223	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-441795P	20030123 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 51 Louisiana Aveue, N.W, WASHINGTON, DC, 20001-2113
NUMBER OF CLAIMS: 61
EXEMPLARY CLAIM: 1
LINE COUNT: 5724
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel hydroxyl compounds, compositions comprising hydroxyl compounds, and methods useful for **treating** and preventing a variety of diseases and conditions such as, but not limited to aging, Alzheimer's Disease, cancer, cardiovascular disease, diabetic nephropathy, diabetic retinopathy, a disorder of glucose metabolism, dyslipidemia, dyslipoproteinemia, hypertension, impotence, inflammation, insulin resistance, lipid elimination in bile, obesity, oxysterol elimination in bile, pancreatitis, pancreatitius, Parkinson's disease, a peroxisome proliferator activated receptor-associated disorder, phospholipid elimination in bile, renal disease, septicemia, metabolic syndrome disorders (e.g., Syndrome X), thrombotic disorder. Compounds and methods of the invention can also be used to modulate C reactive protein or enhance bile production in a patient. In certain embodiments, the compounds, compositions, and methods of the invention are useful in combination **therapy** with other **therapeutics**, such as hypocholesterolemic and hypoglycemic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 9 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2005:36874 USPATFULL
TITLE: Oleaginous pharmaceutical and cosmetic foam
INVENTOR(S): Tamarkin, Dov, Maccabim, ISRAEL
Friedman, Doron, Karmei Yosef, ISRAEL
Eini, Meir, Ness Ziona, ISRAEL
Besonov, Alex, Rehovet, ISRAEL
PATENT ASSIGNEE(S): Foamix Ltd., Ness Ziona, ISRAEL (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005031547	A1	20050210	
APPLICATION INFO.:	US 2004-835505	A1	20040428	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-530015P	20031216 (60)	
	US 2003-492385P	20030804 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WILMER CUTLER PICKERING HALE AND DORR LLP, 60 STATE STREET, BOSTON, MA, 02109

NUMBER OF CLAIMS: 69
EXEMPLARY CLAIM: 1
LINE COUNT: 2357
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to stable oleaginous cosmetic or **therapeutic** foam compositions containing certain active agents, having unique **therapeutic** properties and methods of **treatment** using such compositions. The foamable composition includes at least one solvent selected from a hydrophobic solvent, a silicone oil, an emollient, a co-solvent, and mixtures thereof, wherein the solvent is present at a concentration of about 70% to about 96.5% by weight of the total composition, at least a non-ionic surface-active agent at a concentration of about 0.1% to less than about 10% by weight of the total composition; at least one gelling agent at a concentration of about 0.1% to about 5% by weight of the total composition; a **therapeutically** effective amount of at least one active agent; and at least one liquefied or compressed gas propellant, at a concentration of about 3% to about 25% by weight of the total composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 10 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2005:24105 USPATFULL
TITLE: Novel PPAR agonists, pharmaceutical compositions and uses thereof
INVENTOR(S): Pershadsingh, Harrihar A., Bakersfield, CA, UNITED STATES
Avery, Mitchell A., Oxford, MS, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005020654	A1	20050127	
APPLICATION INFO.:	US 2004-801437	A1	20040315	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-455375P	20030315 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: COOLEY GODWARD, LLP, 3000 EL CAMINO REAL, 5 PALO ALTO SQUARE, PALO ALTO, CA, 94306
NUMBER OF CLAIMS: 92
EXEMPLARY CLAIM: 1
LINE COUNT: 3111
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides novel compounds and pharmaceutical compositions thereof, which at least partially activate PPARγ and may further inhibit the activity of the AT1 receptor. The novel compounds include certain substituted benzimidazole compounds of Formulae I and II, infra. The invention also provides methods of **treating** inflammatory and metabolic disorders and methods for screening compounds for the capability to **treat** or prevent an inflammatory or metabolic disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 11 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2005:17325 USPATFULL

TITLE: Diphenylethylene compounds and uses thereof
INVENTOR(S): Muller, George W., Bridgewater, NJ, UNITED STATES
Payvandi, Faribourz, Belle Mead, NJ, UNITED STATES
Zhang, Ling H., Parsippany, NJ, UNITED STATES
Robarge, Michael J., Burton, OH, UNITED STATES
Chen, Roger, Edison, NJ, UNITED STATES
Man, Hon-Wah, Princeton, NJ, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005014727	A1	20050120	
APPLICATION INFO.:	US 2004-794931	A1	20040305	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-452460P	20030305 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 62
EXEMPLARY CLAIM: 1
LINE COUNT: 8696
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to Diphenylethylene Compounds and compositions comprising a Diphenylethylene Compound. The present invention also relates to methods for preventing or **treating** various diseases and disorders by administering to a subject in need thereof one or more Diphenylethylene Compounds. In particular, the invention relates to methods for preventing or **treating** cancer or an inflammatory disorder by administering to a subject in need thereof one or more Diphenylethylene Compounds. The present invention further relates to articles of manufacture and kits comprising one or more Diphenylethylene Compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 12 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:328111 USPATFULL
TITLE: **Treatment** of neoplasia
INVENTOR(S): Nagarkatti, Leonard C, Richmond, VA, UNITED STATES
Nagarkatti, Prakash, Richmond, VA, UNITED STATES
McKallip, Robert, Richmond, VA, UNITED STATES
Lombard, Catherine, Richmond, VA, UNITED STATES
Ryu, Seongho, Richmond, VA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004259936	A1	20041223	
APPLICATION INFO.:	US 2004-497911	A1	20040813	(10)
	WO 2002-US39310		20021209	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-336732P	20011207 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NIXON & VANDERHYE, PC, 1100 N GLEBE ROAD, 8TH FLOOR, ARLINGTON, VA, 22201-4714
NUMBER OF CLAIMS: 11

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Page(s)
LINE COUNT: 925
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of **treating** a patient in need of **therapy** for an abnormality of cells of the immune system is provided comprising administration of a **therapeutically** effective dose of a compound having CB2 cannabinoid receptor activity. The abnormality is particularly a malignancy such as a leukemia or lymphoma.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 13 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:321517 USPATFULL
TITLE: Method of **treating** nausea, vomiting, retching or any combination thereof
INVENTOR(S): Landau, Steven B., Wellesley, MA, UNITED STATES
Miller, Cheryl L., Natick, MA, UNITED STATES
Thor, Karl B., Morrisville, NC, UNITED STATES
PATENT ASSIGNEE(S): Dynogen, Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004254172	A1	20041216	
APPLICATION INFO.:	US 2004-846979	A1	20040514	(10)
PRIORITY INFORMATION:	US 2003-492478P		20030804	(60) <--
	US 2003-440076P		20030113	(60) <--

RELATED APPLN. INFO.: Continuation of Ser. No. US 2004-757981, filed on 13 Jan 2004, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: CLM-01-70
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1783
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a method of **treating** nausea, vomiting, retching or any combination thereof in a subject in need of **treatment**. The method comprises administering to a subject in need of **treatment** a **therapeutically** effective amount of a compound that has 5-HT.sub.3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of **treating** nausea, vomiting, retching or any combination thereof in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT.sub.3 antagonist and a second amount of a NARI, wherein the first and second amounts together comprise a **therapeutically** effective amount or are each present in a **therapeutically** effective amount. In addition, the method of the invention comprises administering a NARI alone.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 14 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:321516 USPATFULL

TITLE: Method of **treating** nausea, vomiting, retching or any combination thereof
INVENTOR(S): Landau, Steven B., Wellesley, MA, UNITED STATES
Miller, Cheryl L., Natick, MA, UNITED STATES
Thor, Karl B., Morrisville, NC, UNITED STATES
PATENT ASSIGNEE(S): Dynogen, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004254171	A1	20041216
APPLICATION INFO.:	US 2004-846978	A1	20040514 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2004-757981, filed on 13 Jan 2004, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-492478P	20030804 (60)	<--
	US 2003-440076P	20030113 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 89
EXEMPLARY CLAIM: CLM-01-70
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1991
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method of **treating** nausea, vomiting, retching or any combination thereof in a subject in need of **treatment.** The method comprises administering to a subject in need of **treatment** a **therapeutically** effective amount of a compound that has 5-HT.sub.3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of **treating** nausea, vomiting, retching or any combination thereof in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT.sub.3 antagonist and a second amount of a NARI, wherein the first and second amounts together comprise a **therapeutically** effective amount or are each present in a **therapeutically** effective amount. In addition, the method of the invention comprises administering a NARI alone.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 15 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:307917 USPATFULL
TITLE: Cannabinoid derivatives, methods of making, and use thereof
INVENTOR(S): Moore, Bob M., II, Nesbit, MS, UNITED STATES
Ferreira, Antonio M., Memphis, TN, UNITED STATES
Krishnamurthy, Mathangi, Memphis, TN, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004242593	A1	20041202
APPLICATION INFO.:	US 2004-850588	A1	20040520 (10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-472316P	20030520 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edwin V. Merkel, Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051
NUMBER OF CLAIMS: 71
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 2461
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 1'-substituted cannabinoid derivatives of **delta-8-tetrahydrocannabinol**, delta-9-**tetrahydrocannabinol**, and delta-6a-10a-**tetrahydrocannabinol** that have affinity for the cannabinoid receptor type-1 (CB-1) and/or cannabinoid receptor type-2 (CB-2). Compounds having activity as either agonists or antagonists of the CB-1 and/or CB-2 receptors can be used for **treating** CB-1 or CB-2 mediated conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 16 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:292806 USPATFULL
TITLE: Tetracyclic benzamide derivatives and methods of use thereof
INVENTOR(S): Jagtap, Prakash, Beverly, MA, UNITED STATES
Williams, William, Ipswich, MA, UNITED STATES
Nivorozhkin, Alexander, West Roxbury, MA, UNITED STATES
Szabo, Csaba, Gloucester, MA, UNITED STATES
PATENT ASSIGNEE(S): Inotek Pharmaceuticals Corporation (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004229895	A1	20041118	
APPLICATION INFO.:	US 2004-788228	A1	20040226	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-450925P	20030228	(60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WILMER CUTLER PICKERING HALE AND DORR LLP, 300 PARK AVENUE, NEW YORK, NY, 10022
NUMBER OF CLAIMS: 81
EXEMPLARY CLAIM: 1
LINE COUNT: 4566
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to Tetracyclic Benzamide Derivatives; compositions comprising a Tetracyclic Benzamide Derivative; and methods for **treating** or preventing an inflammatory disease, a reperfusion disease, an ischemic condition, renal failure, diabetes, a diabetic complication, a vascular disease, or cancer, comprising administering to a subject in need thereof an effective amount of a Tetracyclic Benzamide Derivative.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 17 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:274385 USPATFULL
TITLE: Dihydroxyl compounds and compositions for cholesterol management and related uses

INVENTOR(S): Dasseux, Jean-Louis Henri, Brighton, MI, UNITED STATES
Oniciu, Carmen Daniela, Ann Arbor, MI, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004214887	A1	20041028	
APPLICATION INFO.:	US 2003-743109	A1	20031223	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-441795P	20030123 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 51 Louisiana Aveue, N.W, WASHINGTON, DC, 20001-2113
NUMBER OF CLAIMS: 50
EXEMPLARY CLAIM: 1
LINE COUNT: 4218
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel dihydroxyl compounds, compositions comprising hydroxyl compounds, and methods useful for **treating** and preventing a variety of diseases and conditions such as, but not limited to aging, Alzheimer's Disease, cancer, cardiovascular disease, diabetic nephropathy, diabetic retinopathy, a disorder of glucose metabolism, dyslipidemia, dyslipoproteinemia, hypertension, impotence, inflammation, insulin resistance, lipid elimination in bile, obesity, oxysterol elimination in bile, pancreatitis, Parkinson's disease, a peroxisome proliferator activated receptor-associated disorder, phospholipid elimination in bile, renal disease, septicemia, metabolic syndrome disorders (e.g., Syndrome X), thrombotic disorder. Compounds and methods of the invention can also be used to modulate C reactive protein or enhance bile production in a patient. In certain embodiments, the compounds, compositions, and methods of the invention are useful in combination **therapy** with other **therapeutics**, such as hypocholesterolemic and hypoglycemic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 18 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:268304 USPATFULL
TITLE: Cycloalkyl-hydroxyl compounds and compositions for cholesterol management and related uses
INVENTOR(S): Dasseux, Jean-Louis Henri, Brighton, MI, UNITED STATES
Oniciu, Carmen Daniela, Ann Arbor, MI, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004209847	A1	20041021	
APPLICATION INFO.:	US 2003-743287	A1	20031223	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-441795P	20030123 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 51 Louisiana Aveue, N.W, WASHINGTON, DC, 20001-2113
NUMBER OF CLAIMS: 57

EXEMPLARY CLAIM: 1
LINE COUNT: 3569
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel cycloalkyl-hydroxyl compounds, compositions comprising hydroxyl compounds, and methods useful for **treating** and preventing a variety of diseases and conditions such as, but not limited to aging, Alzheimer's Disease, cancer, cardiovascular disease, diabetic nephropathy, diabetic retinopathy, a disorder of glucose metabolism, dyslipidemia, dyslipoproteinemia, hypertension, impotence, inflammation, insulin resistance, lipid elimination in bile, obesity, oxysterol elimination in bile, pancreatitis, Parkinson's disease, a peroxisome proliferator activated receptor-associated disorder, phospholipid elimination in bile, renal disease, septicemia, Syndrome X, thrombotic disorder. Compounds and methods of the invention can also be used to modulate C reactive protein or enhance bile production in a patient. In certain embodiments, the compounds, compositions, and methods of the invention are useful in combination **therapy** with other **therapeutics**, such as hypocholesterolemic and hypoglycemic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 19 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:242054 USPATFULL
TITLE: Use of glutamate antagonists for the **treatment** of cancer
INVENTOR(S): Ikonomidou, Hrissanthi, Joersstrasse 16, Berlin, GERMANY, FEDERAL REPUBLIC OF D-13505

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6797692	B1	20040928	
	WO 2000024395		20000504	
APPLICATION INFO.:	US 2001-830354		20010425	(9)
	WO 1999-EP8004		19991022	

	NUMBER	DATE	
PRIORITY INFORMATION:	EP 1998-250380	19981028	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Carlson, Karen Cochrane
ASSISTANT EXAMINER: Desai, Anand
LEGAL REPRESENTATIVE: Millen, White, Zelano & Branigan, P.C.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 802
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Glutamate antagonists (NMDA, AMPA and kainate receptor antagonists) and their physiologically compatible salts can be used for the preparation of drugs for **treatment** of cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 20 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:190737 USPATFULL
TITLE: Method of **treating** nausea, vomiting, retching or any combination thereof

INVENTOR(S): Landau, Steven B., Wellesley, MA, UNITED STATES
Miller, Cheryl L., Natick, MA, UNITED STATES
Thor, Karl B., Morrisville, NC, UNITED STATES
PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., Boston, MA (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004147510	A1	20040729	
APPLICATION INFO.:	US 2004-757981	A1	20040113	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-492478P	20030804 (60)	<--
	US 2003-440076P	20030113 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
NUMBER OF CLAIMS: 70
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 2041
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method of **treating** nausea, vomiting, retching or any combination thereof in a subject in need of **treatment.** The method comprises administering to a subject in need of **treatment** a **therapeutically** effective amount of a compound that has 5-HT.sub.3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of **treating** nausea, vomiting, retching or any combination thereof in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT.sub.3 antagonist and a second amount of a NARI, wherein the first and second amounts together comprise a **therapeutically** effective amount or are each present in a **therapeutically** effective amount. In addition, the method of the invention comprises administering a NARI alone.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 21 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2004:166028 USPATFULL
TITLE: Modulation of anxiety through blockade of anandamide hydrolysis
INVENTOR(S): Piomelli, Daniele, Irvine, CA, UNITED STATES
Duranti, Andrea, Urbino, ITALY
Tontini, Andrea, Pesaro, ITALY
Mor, Marco, Ghedi, ITALY
Tarzia, Giorgio, Petriano, ITALY
PATENT ASSIGNEE(S): The Regents of the University of California, Oakland, CA (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004127518	A1	20040701	
APPLICATION INFO.:	US 2003-681858	A1	20031007	(10)

	NUMBER	DATE

PRIORITY INFORMATION:	US 2002-417008P	20021007 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834	
NUMBER OF CLAIMS:	38	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	3775	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Fatty acid amide hydrolase inhibitors of the Formula: ##STR1##

are provided wherein X is NH, CH.sub.2, O, or S; Q is O or S; Z is O or N; R is an aromatic moiety selected from the group consisting of substituted or unsubstituted aryl; substituted or unsubstituted biphenylyl, substituted or unsubstituted naphthyl, and substituted or unsubstituted phenyl; substituted or unsubstituted terphenylyl; substituted or unsubstituted cycloalkyl, heteroaryl, or alkyl; and R.sub.1 and R.sub.2 are independently selected from the group consisting of H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, and substituted or unsubstituted phenyl, substituted or unsubstituted biphenylyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; with the proviso that if Z is O, one of R.sub.1 and R.sub.2 is absent, and that if Z is N, optionally R.sub.1 and R.sub.2 may optionally be taken together to form a substituted or unsubstituted N-heterocycle or substituted or unsubstituted heteroaryl with the N atom to which they are each attached. Pharmaceutical compositions comprising the compounds of Formula I and methods of using them to inhibit FAAH and/or **treat** appetite disorders, glaucoma, pain, insomnia, and neurological and psychological disorders including anxiety disorders, epilepsy, and depression are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 22 OF 32 USPATFULL on STN

ACCESSION NUMBER:	2004:165953 USPATFULL			
TITLE:	Novel PPAR ligands that do not cause fluid retention, edema or congestive heart failure			
INVENTOR(S):	Pershadsingh, Harrihar A., Bakersfield, CA, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004127443	A1	20040701	
APPLICATION INFO.:	US 2003-627372	A1	20030724	(10)
	NUMBER		DATE	
PRIORITY INFORMATION:	US 2002-402425P		20020810 (60)	<--
	US 2003-455211P		20030315 (60)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	MORRISON & FOERSTER LLP, 755 PAGE MILL RD, PALO ALTO, CA, 94304-1018			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
LINE COUNT:	2675			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods are provided for **treating** or prophylactically preventing metabolic disorders in humans without causing, promoting, or aggravating fluid retention, peripheral edema, pulmonary edema, or congestive heart failure, by administration of a **therapeutically** effective amount of a compound sufficient to partially or fully activate peroxisome proliferator activated receptors (PPARs) and partially or fully inhibit, antagonize or block the activity of angiotensin II type 1 receptors. Metabolic disorders that can be **treated** or prevented include but are not limited to type 2 diabetes, the metabolic syndrome, prediabetes, and other insulin resistance syndromes. Compounds are provided that antagonize or block the angiotensin II type 1 (AT1) receptor, function as partial or full activators of peroxisome proliferator activated receptors (PPARs), can be used to **treat** or prevent diseases known to be **treatable** or preventable by PPAR activators and were not previously recognized to be **therapeutic** targets for angiotensin II receptor antagonists.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 23 OF 32 USPATFULL on STN

ACCESSION NUMBER: 2004:100750 USPATFULL

TITLE: Molecular antigen arrays

INVENTOR(S): Bachmann, Martin F., Seuzach, SWITZERLAND
Tissot, Alain, Zurich, SWITZERLAND
Pumpens, Paul, Riga, LATVIA
Cielens, Indulis, Riga, LATVIA
Renhofa, Regina, Riga, LATVIA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004076611	A1	20040422	
APPLICATION INFO.:	US 2003-617876	A1	20030714	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2002-396126P	20020717 (60)	<--

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., WASHINGTON, DC, 20005

NUMBER OF CLAIMS: 51

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 11 Drawing Page(s)

LINE COUNT: 5340

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a composition comprising an AP205 virus like particle (VLP) and an antigen. The invention also provides a process for producing an antigen or antigenic determinant bound to AP205 VLP. AP205 VLP bound to an antigen is useful in the production of compositions for inducing immune responses that are useful for the prevention or **treatment** of diseases, disorders or conditions including infectious diseases, allergies, cancer, drug addiction, poisoning and to efficiently induce self-specific immune responses, in particular antibody responses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 24 OF 32 USPATFULL on STN

ACCESSION NUMBER: 2004:51617 USPATFULL
TITLE: **Therapy** with cannabinoid compounds for the **treatment** of brain tumors
INVENTOR(S): Guzman Pastor, Manuel, Madrid, SPAIN
Sanchez Garcia, Cristina, Madrid, SPAIN
Galve Roperh, Ismael, Madrid, SPAIN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004039048	A1	20040226
APPLICATION INFO.:	US 2003-647739	A1	20030825 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-958960, filed on 27 Nov 2001, ABANDONED A 371 of International Ser. No. WO 2000-ES450, filed on 22 Nov 2000, UNKNOWN

	NUMBER	DATE	
PRIORITY INFORMATION:	ES 2000-323	20000211	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 469
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The **therapy** with cannabinois in the **treatment** of cerebral tumors involves (intracranial or systematic) administration of (natural of synthetic) cannabinoids to (human or non-human) mammals having cerebral tumors. Activation of the specific receptors of the cannabinoids leads to selective death of the transformed cells. Regression or eradication of the cerebral tumors is achieved without any significant side-effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 25 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:318656 USPATFULL
TITLE: Novel human G-protein coupled receptor, HGPRBMY11, and variants thereof
INVENTOR(S): Barber, Lauren E., Higganum, CT, UNITED STATES
Cacace, Angela, Clinton, CT, UNITED STATES
Feder, John N., Belle Mead, NJ, UNITED STATES
Nelson, Thomas C., Lawrenceville, NJ, UNITED STATES
Bol, David K., Gaithersburg, MD, UNITED STATES
Ramanathan, Chandra, Wallingford, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003224400	A1	20031204
APPLICATION INFO.:	US 2003-369405	A1	20030214 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-991225, filed on 16 Nov 2001, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-249613P	20001117 (60)	<--
	US 2000-257611P	20001221 (60)	<--

US 2001-305818P 20010716 (60) <--
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 15695
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides novel polynucleotides encoding HGPRBMY11 polypeptides, fragments and homologues thereof. The present invention also provides polynucleotides encoding variants of the HGPRBMY11 polypeptide, HGPRBMY11v1 and HGPRBMY11v2. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and **therapeutic** methods for applying these novel HGPRBMY11, HGPRBMY11v1, and/or HGPRBMY11v2 polypeptides to the diagnosis, **treatment**, and/or prevention of various diseases and/or disorders related to these polypeptides, particularly gastrointestinal diseases and/or,disorders, ovarian cancer, and diseases and disorders related to aberrant NFKB modulation. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 26 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:219773 USPATFULL
TITLE: Novel human G-protein coupled receptor, HGPRBMY11, expressed highly in heart and variants thereof
INVENTOR(S): Feder, John N., Belle Mead, NJ, UNITED STATES
Nelson, Thomas C., Lawrenceville, NJ, UNITED STATES
Ramanathan, Chandra S., Wallingford, CT, UNITED STATES
Cacace, Angela M., Clinton, CT, UNITED STATES
Barber, Lauren E., Griswood, CT, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003153063	A1	20030814	<--
APPLICATION INFO.:	US 2001-991225	A1	20011116 (9)	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-249613P	20001117 (60)	<--
	US 2000-257611P	20001221 (60)	<--
	US 2001-305818P	20010716 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 41
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Page(s)
LINE COUNT: 16070
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides novel polynucleotides encoding HGPRBMY11 polypeptides, fragments and homologues thereof. The present invention also provides polynucleotides encoding variants of the HGPRBMY11

polypeptide, HGPRBMY11v1 and HGPRBMY11v2. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and **therapeutic** methods for applying these novel HGPRBMY11, HGPRBMY11v1, and/or HGPRBMY11v2 polypeptides to the diagnosis, **treatment**, and/or prevention of various diseases and/or disorders related to these polypeptides, particularly cardiovascular diseases and/or disorders. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 27 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:188396 USPATFULL
TITLE: P-amidobenzylethers in drug delivery agents
INVENTOR(S): Senter, Peter D., Seattle, WA, UNITED STATES
Toki, Brian E., Everett, WA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003130189	A1	20030710	<--
APPLICATION INFO.:	US 2002-252947	A1	20020923 (10)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-963103, filed on 24 Sep 2001, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS: 106
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 3203
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formulas

L.brket open-st.A.sub.n-Z-X-W.sub.w.brket close-st.D and B.brket open-st.Z-X-W.sub.w.brket close-st.D

wherein: D is a drug moiety; L is a ligand; B is a blocking group; A is an optional acyl unit; Z is an amino acid or a peptide; X is an aminobenzyl ether self-immolative spacer group; W is an optional second self-immolative group; n is an integer of 0 or 1; and w is an integer of 0 or 1, and compositions of said compounds with pharmaceutically acceptable carrier, diluent and/or excipient, and methods of delivery the drug D via the compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 28 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:160082 USPATFULL
TITLE: Novel phosphoramidate compounds and methods of use
INVENTOR(S): Shepard, H. Michael, Encinitas, CA, UNITED STATES
Vaino, Andrew Rein, San Diego, CA, UNITED STATES
Lehsten, Danielle M., San Diego, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003109697	A1	20030612	<--

APPLICATION INFO.: US 2002-119927 A1 20020409 (10)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-782721, filed on 12 Feb 2001, PENDING Continuation of Ser. No. US 1999-235961, filed on 22 Jan 1999, GRANTED, Pat. No. US 6339151

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-72264P	19980123 (60)	<--
	US 1998-76950P	19980305 (60)	<--
	US 1998-108634P	19981116 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 3503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides compounds, compositions and methods for **treating** cancer, infectious disease, an autoimmune disorder or an inflammatory condition. **Therapeutic** compounds useful in the methods of this invention are 5'-phosphoramidatyl, 1,5-substituted pyrimidine compounds, derivatives, analogs and pharmaceutically acceptable salts thereof

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 29 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:145924 USPATFULL
TITLE: Packaging of immunostimulatory substances into virus-like particles: method of preparation and use
INVENTOR(S): Bachmann, Martin, Winterthur, SWITZERLAND
Storni, Tazio, Viganello, SWITZERLAND
Maurer, Patrik, Winterthur, SWITZERLAND
Tissot, Alain, Zurich, SWITZERLAND
Schwarz, Katrin, Schlieren, SWITZERLAND
Meijerink, Edwin, Zurich, SWITZERLAND
Lipowsky, Gerd, Zurich, SWITZERLAND
Pumpens, Paul, Riga, LATVIA
Cielens, Indulis, Riga, LATVIA
Renhofa, Regina, Riga, LATVIA
PATENT ASSIGNEE(S): Cytos Biotechnology AG (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003099668	A1	20030529	<--
APPLICATION INFO.:	US 2002-244065	A1	20020916 (10)	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-318994P	20010914 (60)	<--
	US 2002-374145P	20020422 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., SUITE 600, WASHINGTON, DC, 20005-3934
NUMBER OF CLAIMS: 207

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 60 Drawing Page(s)
LINE COUNT: 7907
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the finding that virus like particles (VLPs) can be loaded with immunostimulatory substances, in particular with DNA oligonucleotides containing non-methylated C and G (CpGs). Such CpG-VLPs are dramatically more immunogenic than their CpG-free counterparts and induce enhanced B and T cell responses. The immune response against antigens optionally coupled, fused or attached otherwise to the VLPs is similarly enhanced as the immune response against the VLP itself. In addition, the T cell responses against both the VLPs and antigens are especially directed to the Th1 type. Antigens attached to CpG-loaded VLPs may therefore be ideal vaccines for prophylactic or **therapeutic** vaccination against allergies, tumors and other self-molecules and chronic viral diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 30 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:133508 USPATFULL
TITLE: In vivo activation of antigen presenting cells for enhancement of immune responses induced by virus like particles
INVENTOR(S): Bachmann, Martin F., Winterthur, SWITZERLAND
Lechner, Franziska, Zurich, SWITZERLAND
Storni, Tazio, Viganello, SWITZERLAND
PATENT ASSIGNEE(S): Cytos Biotechnology AG (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003091593	A1	20030515	<--
APPLICATION INFO.:	US 2002-243739	A1	20020916 (10)	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-318967P	20010914 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., SUITE 600, WASHINGTON, DC, 20005-3934
NUMBER OF CLAIMS: 194
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 20 Drawing Page(s)
LINE COUNT: 6522
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the finding that stimulation of antigen presenting cell (APC) activation using substances such as anti-CD40 antibodies or DNA oligomers rich in non-methylated C and G (CpGs) can dramatically enhance the specific T cell response obtained after vaccination with recombinant virus like particles (VLPs) coupled, fused or otherwise attached to antigens. While vaccination with recombinant VLPs fused to a cytotoxic T cell (CTL) epitope of lymphocytic choriomeningitis virus induced low levels cytolytic activity only and did not induce efficient anti-viral protection, VLPs injected together with anti-CD40 antibodies or CpGs induced strong CTL activity and full anti-viral protection. Thus, stimulation of APC-activation through antigen presenting cell activators such as anti-CD40 antibodies or CpGs can exhibit a potent adjuvant effect for vaccination with VLPs coupled,

fused or attached otherwise to antigens.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 31 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:86801 USPATFULL
TITLE: Polynucleotide encoding a novel human G-protein coupled receptor, HGPRBMY25, expressed highly in immune-related tissues
INVENTOR(S): Ramanathan, Chandra S., Wallingford, CT, UNITED STATES
Feder, John N., Belle Mead, NJ, UNITED STATES
Mintier, Gabriel A., Hightstown, NJ, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003060409	A1	20030327	<--
APPLICATION INFO.:	US 2002-81775	A1	20020221	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-270134P	20010221 (60)	<--
	US 2001-278952P	20010327 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 13055
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides novel polynucleotides encoding HGPRBMY25 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and **therapeutic** methods for applying these novel HGPRBMY25 polypeptides to the diagnosis, **treatment**, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L36 ANSWER 32 OF 32 USPATFULL on STN
ACCESSION NUMBER: 2003:71937 USPATFULL
TITLE: **Treatment** of glial tumors with glutamate antagonists
INVENTOR(S): Nedergaard, Maiken, South Salem, NY, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003050224	A1	20030313	<--
APPLICATION INFO.:	US 2002-225396	A1	20020820	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-313030P	20010820 (60)	<--

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1303
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a method of **treating** glial tumors in a subject, which includes providing a glutamate antagonist or a NMDA receptor antagonist and administering the glutamate antagonist or NMDA receptor antagonist to a subject with a glial tumor of the brain or spinal cord under conditions effective to **treat** the glial tumor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> d his ful

     FILE 'HCAPLUS' ENTERED AT 12:20:01 ON 26 JUL 2005
                  E PASTOR MANUEL GUZMAN/AU
L1             43 SEA ABB=ON  ("PASTOR MANUEL"/AU OR "PASTOR MANUEL G"/AU)
                  E GARCIA CRISTINA SANCHEZ/AU
L2              3 SEA ABB=ON  ("GARCIA CRISTINA LEONOR"/AU OR "GARCIA CRISTINA
                  ROMERO AVILA"/AU OR "GARCIA CRISTINA SANCHEZ"/AU OR "GARCIA
                  CRISTINA TORRES"/AU)
                  E ROPERH ISMAEL GALVE/AU
L3              0 SEA ABB=ON  L1 AND L2
L4             46 SEA ABB=ON  L1 OR L2
L5              0 SEA ABB=ON  L4 AND ?CANNABINOID?
L6              0 SEA ABB=ON  L4 AND ?TUMOR?
L7              4 SEA ABB=ON  L4 AND ?BRAIN?
L8              0 SEA ABB=ON  L4 AND ?CANNAB?
L9              0 SEA ABB=ON  L1 AND ?CANCER?
L10             0 SEA ABB=ON  L1 AND ?TUMOR?
                  E GUZMAN MANUEL/AU
L11            76 SEA ABB=ON  "GUZMAN MANUEL"/AU
                  E SANCHEZ CRISTINA/AU
L12            43 SEA ABB=ON  ("SANCHEZ CRISTIAN G"/AU OR "SANCHEZ CRISTINA"/AU)
                  E GALVE ROPERH ISMAEL/AU
L13            29 SEA ABB=ON  ("GALVE ROPERH I"/AU OR "GALVE ROPERH ISMAEL"/AU)
L14            10 SEA ABB=ON  L11 AND L12 AND L13
L15             9 SEA ABB=ON  L14 AND ?CANNAB?
L16             4 SEA ABB=ON  L15 AND ?BRAIN?
L17               ANALYZE L16 1-4 CT :      16 TERMS
                  SELECT RN L16 1-4

     FILE 'REGISTRY' ENTERED AT 13:09:39 ON 26 JUL 2005
L18             4 SEA ABB=ON  (112830-95-2/BI OR 1972-08-3/BI OR 259869-55-1/BI
                  OR 9068-41-1/BI)

     FILE 'HCAPLUS' ENTERED AT 13:09:48 ON 26 JUL 2005
L19             2 SEA ABB=ON  L16 AND L18

     FILE 'REGISTRY' ENTERED AT 13:12:57 ON 26 JUL 2005
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                  E Δ8-TETRAHYDROCANNABINOL/CN
L20             1 SEA ABB=ON  Δ8-TETRAHYDROCANNABINOL/CN
L21             2 SEA ABB=ON  (CANNABINOL OR CANNABIDIOL)/CN
L22             3 SEA ABB=ON  L20 OR L21

     FILE 'HCAPLUS' ENTERED AT 13:14:23 ON 26 JUL 2005
L23          5906 SEA ABB=ON  L22 OR (Δ8-TETRAHYDROCANNABINOL? OR ?CANNABIN
                  OL? OR ?CANNABIDIOL?)
L24            68 SEA ABB=ON  L23 AND (?BLASTOMA? OR ?EPITHELOMA? OR ?GERMINOMA?
                  OR ?CARCINOMA? OR ?ASTROCYTOMA? OR ?EPENDYMOMA? OR ?OLIGODENROG
                  LIOMA? OR ?OLIGODENDROGLIOMA? OR ?NEUROEPITHELOMA? OR ?NEUROECT
                  ODERM?(W)(?TUMOR? OR ?TUMOUR?) OR ?MENINGIOMA? OR ?SARCOMA? OR
                  ?MELANOMA? OR ?SCHWANOMA?)
L25            29 SEA ABB=ON  L24 AND (?THERAP? OR ?TREAT? OR ?CURE? OR ?IMPROV?)
L26            26 SEA ABB=ON  L25 AND (PRD<20030825 OR PD<20030825)
                                                    26 cits from CA Plus
     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
     13:19:45 ON 26 JUL 2005
L27           150 SEA ABB=ON  L25
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L28 74 DUP REMOV L27 (76 DUPLICATES REMOVED)
L29 29 SEA ABB=ON L28 AND (?GLIOBLASTOMA? OR ?MEDUL?(W) ?EPITHELOMA? OR ?MEDULOBLASTOMA? OR ?NEUROBLASTOMA? OR ?GERMINOMA? OR ?EMBROYOCARCINOMA? OR ?ASTROCYTOMA? OR ?ASTROBLASTOMA? OR ?EPENDYMOMA? OR ?OLIGODENROGLIOMA? OR ?PLEXOCARCINOMA? OR ?NEUROEPITHELOMA? OR ?PINEOBLASTOMA? OR ?EPANDIMOBLASTOMA?)
L30 1 SEA ABB=ON L28 AND (?NEUROECTODERM?(W)(?TUMOR? OR ?TUMOUR?) OR ?MALIGN?(W)(?MENINGIOMA? OR ?MELANOMA? OR ?SCHWANOMA?) OR ?CHONDROSARCOMA? OR ?MENINGEAL?(W) ?SARCOM?)
L31 30 SEA ABB=ON L29 OR L30 30 citations above db's

FILE 'USPATFULL' ENTERED AT 13:25:51 ON 26 JUL 2005
L32 60 SEA ABB=ON L27 AND (?GLIOBLASTOMA? OR ?MEDUL?(W)?EPITHELOMA? OR ?MEDULOBLASTOMA? OR ?NEUROBLASTOMA? OR ?GERMINOMA? OR ?EMBROYOCARCINOMA? OR ?ASTROCYTOMA? OR ?ASTROBLASTOMA? OR ?EPENDYMOMA? OR ?OLIGODENROGLIOMA? OR ?PLEXOCARCINOMA? OR ?NEUROEPITHELOMA? OR ?PINEOBLASTOMA? OR ?EPANDIMOBLASTOMA?)
L33 32 SEA ABB=ON L27 AND (?NEUROECTODERM?(W)(?TUMOR? OR ?TUMOUR?) OR ?MALIGN?(W)(?MENINGIOMA? OR ?MELANOMA? OR ?SCHWANOMA?) OR ?CHONDROSARCOMA? OR ?MENINGEAL?(W)?SARCOM?)
L34 63 SEA ABB=ON L32 OR L33
L35 51 SEA ABB=ON L34 AND (PRD<20030825 OR PD<20030825)
L36 32 SEA ABB=ON L35 AND ?TREAT?(5A)?THERAP? 32 citations from USPATFULL

FILE HCAPLUS

FILE COVERS 1907 - 26 Jul 2005 VOL 143 ISS 5
FILE LAST UPDATED: 25 Jul 2005 (20050725/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 JUL 2005 HIGHEST RN 856925-80-9
DICTIONARY FILE UPDATES: 25 JUL 2005 HIGHEST RN 856925-80-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE MEDLINE
FILE LAST UPDATED: 23 JUL 2005 (20050723/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CANCERLIT
FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 July 2005 (20050721/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 21 Jul 2005 (20050721/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 4 JUL 2005 <20050704/UP>
FILE COVERS APR 1973 TO MARCH 31, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS
FILE COVERS 1985 TO 25 JUL 2005 (20050725/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Jul 2005 (20050726/PD)
FILE LAST UPDATED: 26 Jul 2005 (20050726/ED)
HIGHEST GRANTED PATENT NUMBER: US6922846
HIGHEST APPLICATION PUBLICATION NUMBER: US2005160510
CA INDEXING IS CURRENT THROUGH 26 Jul 2005 (20050726/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Jul 2005 (20050726/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

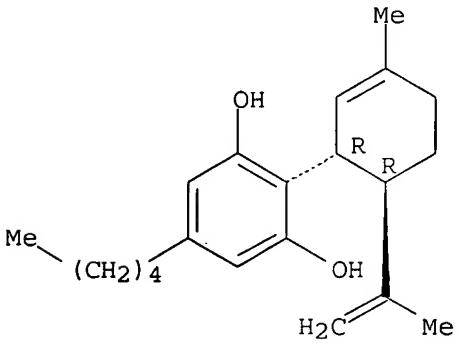
>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l22 1-3

L22 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN 13956-29-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,3-Benzenediol, 2-[(1R,6R)-3-methyl-6-(1-methylethenyl)-2-cyclohexen-1-yl]-5-pentyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Benzenediol, 2-[3-methyl-6-(1-methylethenyl)-2-cyclohexen-1-yl]-5-pentyl-, (1R-trans)-
CN **Cannabidiol (7CI)**
CN Resorcinol, 2-p-mentha-1,8-dien-3-yl-5-pentyl-, trans-(-)- (8CI)
OTHER NAMES:
CN (-)-Cannabidiol
CN (-)-trans-Cannabidiol
CN Δ1(2)-trans-Cannabidiol
CN CBD
FS STEREOSEARCH
DR 521-37-9, 18436-46-9, 20547-66-4
MF C21 H30 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IMSRESEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



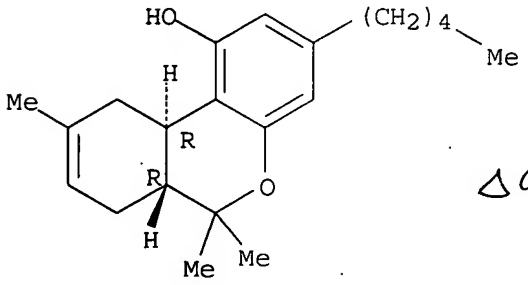
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

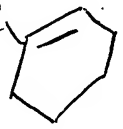
1074 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1077 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
ED Entered STN: 16 Nov 1984

L22 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN 5957-75-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN 6H-Dibenzo[b,d]pyran-1-ol, 6a,7,10,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-

, (6aR,10aR)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6H-Dibenzo[b,d]pyran-1-ol, 6a,7,10,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-, (6aR-trans)-
CN 6H-Dibenzo[b,d]pyran-1-ol, 6a,7,10,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-, trans-(-)- (8CI)
OTHER NAMES:
CN (-)-Δ6-Tetrahydrocannabinol
CN (-)-Δ8-6a,10a-trans-Tetrahydrocannabinol
CN (-)-Δ8-Tetrahydrocannabinol
CN (-)-Δ8-THC
CN (-)-Δ8-trans-Tetrahydrocannabinol
CN (-)-trans-Δ8-Tetrahydrocannabinol
CN Δ1(6)-Tetrahydrocannabinol
CN Δ1(6)-trans-Tetrahydrocannabinol
CN Δ6-Tetrahydrocannabinol
CN Δ8-1-Tetrahydrocannabinol
CN **Δ8-Tetrahydrocannabinol**
CN Δ8-THC
CN Δ8-trans-Tetrahydrocannabinol
CN Cannabinol, Δ1(6)-tetrahydro-
CN 1-Δ8-Tetrahydrocannabinol
CN NSC 134453
CN trans-Δ8-Tetrahydrocannabinol
FS STEREOSEARCH
DR 6465-29-8, 6909-11-1, 1397-08-6, 17766-01-7, 23057-16-1, 1972-07-2
MF C21 H30 O2
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



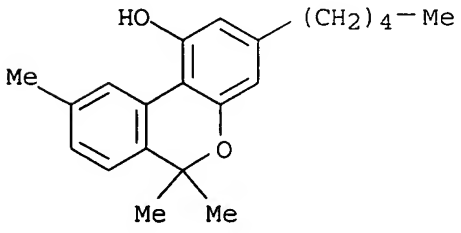
Δ9 - only difference is 

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

611 REFERENCES IN FILE CA (1907 TO DATE)
28 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
611 REFERENCES IN FILE CAPLUS (1907 TO DATE)
ED Entered STN: 16 Nov 1984

L22 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN 521-35-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN 6H-Dibenzo[b,d]pyran-1-ol, 6,6,9-trimethyl-3-pentyl- (7CI, 8CI, 9CI) (CA

INDEX NAME)
OTHER CA INDEX NAMES:
CN **Cannabinol** (6CI)
OTHER NAMES:
CN 3-Amyl-1-hydroxy-6,6,9-trimethyl-6H-dibenzo[b,d]pyran
CN 6,6,9-Trimethyl-3-pentyl-6H-dibenzo[b,d]pyran-1-ol
CN CBN
CN NSC 134455
FS 3D CONCORD
DR 47276-71-1
MF C21 H26 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

871 REFERENCES IN FILE CA (1907 TO DATE)
23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
871 REFERENCES IN FILE CAPLUS (1907 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
ED Entered STN: 16 Nov 1984

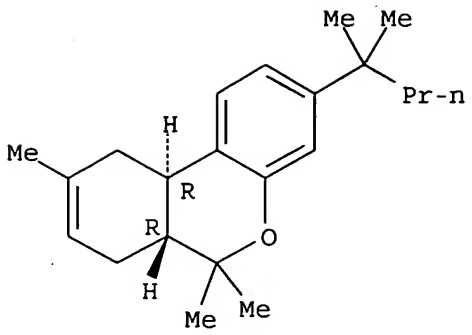
=> d ibib abs hitstr ind l19 1-2

L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:584375 HCAPLUS
DOCUMENT NUMBER: 135:338839
TITLE: Inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor
AUTHOR(S): **Sanchez, Cristina**; de Ceballos, Maria L.; Gomez del Pulgar, Teresa; Rueda, Daniel; Corbacho, Cesar; Velasco, Guillermo; **Galve-Roperh, Ismael**; Huffman, John W.; Ramon y Cajal, Santiago; **Guzman, Manuel**
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: Cancer Research (2001), 61(15), 5784-5789
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of new therapeutic strategies is essential for the management of gliomas, one of the most malignant forms of cancer. We have shown previously that the growth of the rat glioma C6 cell line is inhibited by psychoactive **cannabinoids.** These compds. act on the **brain** and some other organs through the widely expressed CB1 receptor. By contrast, the other **cannabinoid** receptor subtype, the CB2 receptor, shows a much more restricted distribution and is absent from normal **brain.** Here we show that local administration of the selective CB2 agonist JWH-133 at 50 μg/day to Rag-2-/- mice induced a considerable regression of malignant tumors generated by inoculation of C6 glioma cells. The selective involvement of the CB2 receptor in this action was evidenced by: (a) the prevention by the CB2 antagonist SR144528 but not the CB1 antagonist SR141716; (b) the down-regulation of the CB2 receptor but not the CB1 receptor in the tumors; and (c) the absence of typical CB1-mediated psychotropic side effects. **Cannabinoid** receptor expression was subsequently examined in biopsies from human astrocytomas. A full 70% (26 of 37) of the human astrocytomas analyzed expressed significant levels of **cannabinoid** receptors. Of interest, the extent of CB2 receptor expression was directly related with tumor malignancy. In addition, the growth of grade IV human astrocytoma cells in Rag-2-/- mice was completely blocked by JWH-133 administration at 50 μg/day. Expts. carried out with C6 glioma cells in culture evidenced the internalization of the CB2 but not the CB1 receptor upon JWH-133 challenge and showed that selective activation of the CB2 receptor signaled apoptosis via enhanced ceramide synthesis de novo. These results support a therapeutic approach for the treatment of malignant gliomas devoid of psychotropic side effects.

IT **259869-55-1**, JWH 133
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(JWH 133; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
RN 259869-55-1 HCAPLUS
CN 6H-Dibenzo[b,d]pyran, 3-(1,1-dimethylbutyl)-6a,7,10,10a-tetrahydro-6,6,9-trimethyl-, (6aR,10aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-6 (Pharmacology)
ST JWH133 antitumor glioma CB2 **cannabinoid** receptor
IT **Cannabinoid** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CB1; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT **Cannabinoid** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CB2; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT Astrocyte
(astrocytoma, inhibitors; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT Antitumor agents
(astrocytoma; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**cannabinoid** CB2; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT Neuroglia
(glioma, inhibitors; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT Antitumor agents
(glioma; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT Apoptosis
(inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
IT **259869-55-1**, JWH 133
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(JWH 133; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:214754 HCAPLUS
DOCUMENT NUMBER: 131:27842
TITLE: The stimulation of ketogenesis by **cannabinoids** in cultured astrocytes defines carnitine

palmitoyltransferase I as a new ceramide-activated enzyme

AUTHOR(S): Blazquez, Cristina; **Sanchez, Cristina**; Daza, Andres; **Galve-Roperh, Ismael**; **Guzman, Manuel**

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain

SOURCE: Journal of Neurochemistry (1999), 72(4), 1759-1768
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of **cannabinoids** on ketogenesis in primary cultures of rat astrocytes were studied. Δ9- **Tetrahydrocannabinol** (THC), the major active component of marijuana, produced a malonyl-CoA-independent stimulation of carnitine palmitoyltransferase I (CPT-I) and ketogenesis from [14C]palmitate. The THC-induced stimulation of ketogenesis was mimicked by the synthetic **cannabinoid** HU-210 and was prevented by pertussis toxin and the CB1 **cannabinoid** receptor antagonist SR141716. Expts. performed with different cellular modulators indicated that the THC-induced stimulation of ketogenesis was independent of cAMP, Ca2+, protein kinase C, and mitogen-activated protein kinase (MAPK). The possible involvement of ceramide in the activation of ketogenesis by **cannabinoids** was subsequently studied. THC produced a CB1 receptor-dependent stimulation of sphingomyelin breakdown that was concomitant to an elevation of intracellular ceramide levels. Addition of exogenous sphingomyelinase to the astrocyte culture medium led to a MAPK-independent activation of ketogenesis that was quant. similar and not additive to that exerted by THC. Furthermore, ceramide activated CPT-I in astrocyte mitochondria. Results thus indicate that **cannabinoids** stimulate ketogenesis in astrocytes by a mechanism that may rely on CB1 receptor activation, sphingomyelin hydrolysis, and ceramide-mediated activation of CPT-I.

IT **9068-41-1**, Carnitine palmitoyltransferase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(I; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)

RN 9068-41-1 HCAPLUS

CN Palmitoyltransferase, carnitine (9CI) (CA INDEX NAME)

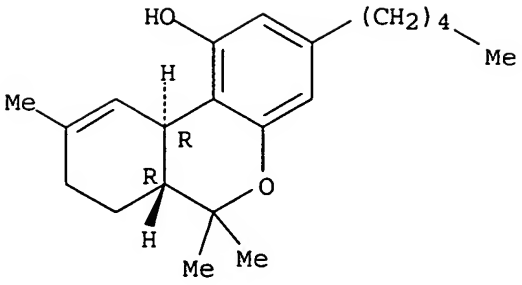
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **1972-08-3**, Δ9- **Tetrahydrocannabinol**
112830-95-2, HU-210
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)

RN 1972-08-3 HCAPLUS

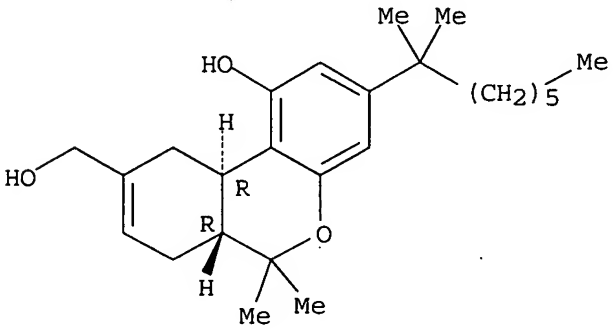
CN 6H-Dibenzo[b,d]pyran-1-ol, 6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-, (6aR,10aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 112830-95-2 HCAPLUS
CN 6H-Dibenzo[b,d]pyran-9-methanol, 3-(1,1-dimethylheptyl)-6a,7,10,10a-tetrahydro-1-hydroxy-6,6-dimethyl-, (6aR,10aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-11 (Pharmacology)
Section cross-reference(s): 2
ST **cannabinoid** receptor astrocyte ketogenesis carnitine palmitoyltransferase; **tetrahydrocannabinol** sphingomyelin ceramide palmitoyltransferase astrocyte ketogenesis; signal transduction **cannabinoid** astrocyte metab
IT **Cannabinoid** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CB1, activation of; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Astrocyte
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Ceramides
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT **Cannabinoids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Ketone bodies

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)

IT Energy metabolism, animal
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis in relation to **brain** energy metabolism)

IT Signal transduction, biological
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis in relation to signal transduction)

IT Sphingomyelins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hydrolysis of; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)

IT **9068-41-1**, Carnitine palmitoyltransferase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(I; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)

IT **1972-08-3**, Δ9- **Tetrahydrocannabinol**
112830-95-2, HU-210
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs ind l16 1-4

L16 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:604067 HCAPLUS
DOCUMENT NUMBER: 141:199325
TITLE: Hypothesis: **cannabinoid** therapy for the treatment of gliomas?
AUTHOR(S): Velasco, Guillermo; **Galve-Roperh, Ismael**; **Sanchez, Cristina**; Blazquez, Cristina; **Guzman, Manuel**
CORPORATE SOURCE: School of Biology, Department of Biochemistry and Molecular Biology I, Complutense University, Madrid, 28040, Spain
SOURCE: Neuropharmacology (2004), 47(3), 315-323
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Gliomas, in particular glioblastoma multiforme or grade IV astrocytoma, are the most frequent class of malignant primary **brain** tumors and one of the most aggressive forms of cancer. Current therapeutic strategies for the treatment of glioblastoma multiforme are usually ineffective or just palliative. During the last few years, several studies have shown that **cannabinoids**-the active components of the plant **Cannabis** sativa and their derivs.-slow the growth of different types of tumors, including gliomas, in laboratory animals. **Cannabinoids** induce apoptosis of glioma cells in culture via sustained ceramide accumulation, extracellular signal-regulated kinase activation and Akt inhibition. In addition, **cannabinoid** treatment inhibits angiogenesis of gliomas in vivo. Remarkably, **cannabinoids** kill glioma cells selectively and can protect non-transformed glial cells from death. These and other findings reviewed here might set the basis for a potential use of **cannabinoids** in the management of gliomas.
CC 1-0 (Pharmacology)
ST review antitumor **cannabinoid** glioma therapy
IT Antitumor agents
Neuroglia, neoplasm
(**cannabinoid** therapy for treatment of gliomas)
IT **Cannabinoids**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cannabinoid** therapy for treatment of gliomas)
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:584375 HCAPLUS
DOCUMENT NUMBER: 135:338839
TITLE: Inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor
AUTHOR(S): **Sanchez, Cristina**; de Ceballos, Maria L.; Gomez del Pulgar, Teresa; Rueda, Daniel; Corbacho, Cesar; Velasco, Guillermo; **Galve-Roperh, Ismael**; Huffman, John W.; Ramon y Cajal, Santiago; **Guzman, Manuel**
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain

SOURCE: Cancer Research (2001), 61(15), 5784-5789
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of new therapeutic strategies is essential for the management of gliomas, one of the most malignant forms of cancer. We have shown previously that the growth of the rat glioma C6 cell line is inhibited by psychoactive **cannabinoids.** These compds. act on the **brain** and some other organs through the widely expressed CB1 receptor. By contrast, the other **cannabinoid** receptor subtype, the CB2 receptor, shows a much more restricted distribution and is absent from normal **brain.** Here we show that local administration of the selective CB2 agonist JWH-133 at 50 μg/day to Rag-2-/- mice induced a considerable regression of malignant tumors generated by inoculation of C6 glioma cells. The selective involvement of the CB2 receptor in this action was evidenced by: (a) the prevention by the CB2 antagonist SR144528 but not the CB1 antagonist SR141716; (b) the down-regulation of the CB2 receptor but not the CB1 receptor in the tumors; and (c) the absence of typical CB1-mediated psychotropic side effects. **Cannabinoid** receptor expression was subsequently examined in biopsies from human astrocytomas. A full 70% (26 of 37) of the human astrocytomas analyzed expressed significant levels of **cannabinoid** receptors. Of interest, the extent of CB2 receptor expression was directly related with tumor malignancy. In addition, the growth of grade IV human astrocytoma cells in Rag-2-/- mice was completely blocked by JWH-133 administration at 50 μg/day. Expts. carried out with C6 glioma cells in culture evidenced the internalization of the CB2 but not the CB1 receptor upon JWH-133 challenge and showed that selective activation of the CB2 receptor signaled apoptosis via enhanced ceramide synthesis de novo. These results support a therapeutic approach for the treatment of malignant gliomas devoid of psychotropic side effects.

CC 1-6 (Pharmacology)
ST JWH133 antitumor glioma CB2 **cannabinoid** receptor

IT **Cannabinoid** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CB1; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT **Cannabinoid** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CB2; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT Astrocyte
(astrocytoma, inhibitors; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT Antitumor agents
(astrocytoma; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**cannabinoid** CB2; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT Neuroglia
(glioma, inhibitors; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT Antitumor agents

(glioma; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT Apoptosis
(inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

IT 259869-55-1, JWH 133
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(JWH 133; inhibition of glioma growth in vivo by selective activation of the CB2 **cannabinoid** receptor)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:223917 HCAPLUS
DOCUMENT NUMBER: 135:189491
TITLE: Control of the cell survival/death decision by **cannabinoids**
AUTHOR(S): **Guzman, Manuel**; **Sanchez, Cristina**; **Galve-Roperh, Ismael**
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: Journal of Molecular Medicine (Berlin, Germany) (2000), 78(11), 613-625
CODEN: JMLME8; ISSN: 0946-2716
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 114 refs. **Cannabinoids**, the active components of **Cannabis** sativa (marijuana), and their derivs. produce a wide spectrum of central and peripheral effects, some of which may have clin. application. The discovery of specific **cannabinoid** receptors and a family of endogenous ligands of those receptors has attracted much attention to **cannabinoids** in recent years. One of the most exciting and promising areas of current **cannabinoid** research is the ability of these compds. to control the cell survival/death decision. Thus **cannabinoids** may induce proliferation, growth arrest, or apoptosis in a number of cells, including neurons, lymphocytes, and various transformed neural and nonneural cells. The variation in drug effects may depend on exptl. factors such as drug concentration, timing of drug delivery, and type of cell examined Regarding the central nervous system, most of the exptl. evidence indicates that **cannabinoids** may protect neurons from toxic insults such as glutamatergic over-stimulation, ischemia and oxidative damage. In contrast, **cannabinoids** induce apoptosis of glioma cells in culture and regression of malignant gliomas in vivo. Breast and prostate cancer cells are also sensitive to **cannabinoid** -induced antiproliferation. Regarding the immune system, low doses of **cannabinoids** may enhance cell proliferation, whereas high doses of **cannabinoids** usually induce growth arrest or apoptosis. The neuroprotective effect of **cannabinoids** may have potential clin. relevance for the treatment of neurodegenerative disorders such as multiple sclerosis, Parkinson's disease, and ischemia/stroke, whereas their growth-inhibiting action on transformed cells might be useful for the management of malignant **brain** tumors. Ongoing investigation is in search for **cannabinoid**-based therapeutic strategies devoid of non-desired psychotropic effects.

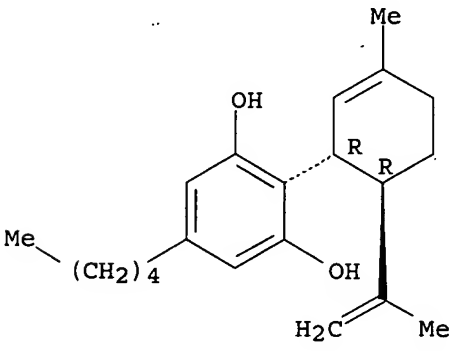
CC 1-0 (Pharmacology)
ST review **cannabinoid** cell proliferation apoptosis
IT Antitumor agents
Apoptosis
Cell proliferation
Proliferation inhibition
(**cannabinoids** role cell survival or death decision and relation to therapeutic strategies)
IT **Cannabinoids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cannabinoids** role cell survival or death decision and relation to therapeutic strategies)
IT Cytoprotective agents
(neuroprotectants; **cannabinoids** role cell survival or death decision and relation to therapeutic strategies)
REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:214754 HCAPLUS
DOCUMENT NUMBER: 131:27842
TITLE: The stimulation of ketogenesis by **cannabinoids** in cultured astrocytes defines carnitine palmitoyltransferase I as a new ceramide-activated enzyme
AUTHOR(S): Blazquez, Cristina; **Sanchez, Cristina**; Daza, Andres; **Galve-Roperh, Ismael**; **Guzman, Manuel**
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: Journal of Neurochemistry (1999), 72(4), 1759-1768
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of **cannabinoids** on ketogenesis in primary cultures of rat astrocytes were studied. Δ9- **Tetrahydrocannabinol** (THC), the major active component of marijuana, produced a malonyl-CoA-independent stimulation of carnitine palmitoyltransferase I (CPT-I) and ketogenesis from [14C]palmitate. The THC-induced stimulation of ketogenesis was mimicked by the synthetic **cannabinoid** HU-210 and was prevented by pertussis toxin and the CB1 **cannabinoid** receptor antagonist SR141716. Expts. performed with different cellular modulators indicated that the THC-induced stimulation of ketogenesis was independent of cAMP, Ca2+, protein kinase C, and mitogen-activated protein kinase (MAPK). The possible involvement of ceramide in the activation of ketogenesis by **cannabinoids** was subsequently studied. THC produced a CB1 receptor-dependent stimulation of sphingomyelin breakdown that was concomitant to an elevation of intracellular ceramide levels. Addition of exogenous sphingomyelinase to the astrocyte culture medium led to a MAPK-independent activation of ketogenesis that was quant. similar and not additive to that exerted by THC. Furthermore, ceramide activated CPT-I in astrocyte mitochondria. Results thus indicate that **cannabinoids** stimulate ketogenesis in astrocytes by a mechanism that may rely on CB1 receptor activation, sphingomyelin hydrolysis, and

ceramide-mediated activation of CPT-I.
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
ST **cannabinoid** receptor astrocyte ketogenesis carnitine palmitoyltransferase; **tetrahydrocannabinol** sphingomyelin ceramide palmitoyltransferase astrocyte ketogenesis; signal transduction **cannabinoid** astrocyte metab
IT **Cannabinoid** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CB1, activation of; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Astrocyte
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Ceramides
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT **Cannabinoids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Ketone bodies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT Energy metabolism, animal
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis in relation to **brain** energy metabolism)
IT Signal transduction, biological
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis in relation to signal transduction)
IT Sphingomyelins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hydrolysis of; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT 9068-41-1, Carnitine palmitoyltransferase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(I; carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
IT 1972-08-3, Δ9- **Tetrahydrocannabinol** 112830-95-2, HU-210
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(carnitine palmitoyltransferase I as ceramide-activated enzyme in **cannabinoids** stimulation of astrocyte ketogenesis)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 17 REGISTRY COPYRIGHT 2005 ACS on STN
RN 13956-29-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,3-Benzenediol, 2-[(1R,6R)-3-methyl-6-(1-methylethenyl)-2-cyclohexen-1-yl]-5-pentyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Benzenediol, 2-[3-methyl-6-(1-methylethenyl)-2-cyclohexen-1-yl]-5-pentyl-, (1R-trans)-
CN **Cannabidiol (7CI)**
CN Resorcinol, 2-p-mentha-1,8-dien-3-yl-5-pentyl-, trans-(-)- (8CI)
OTHER NAMES:
CN **(-)-Cannabidiol**
CN **(-)-trans-Cannabidiol**
CN **Δ1(2)-trans-Cannabidiol**
CN CBD
FS STEREOSEARCH
DR 521-37-9, 18436-46-9, 20547-66-4
MF C21 H30 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IMSRESEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



514/729
239
(+)
H2C Me

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1072 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1075 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)